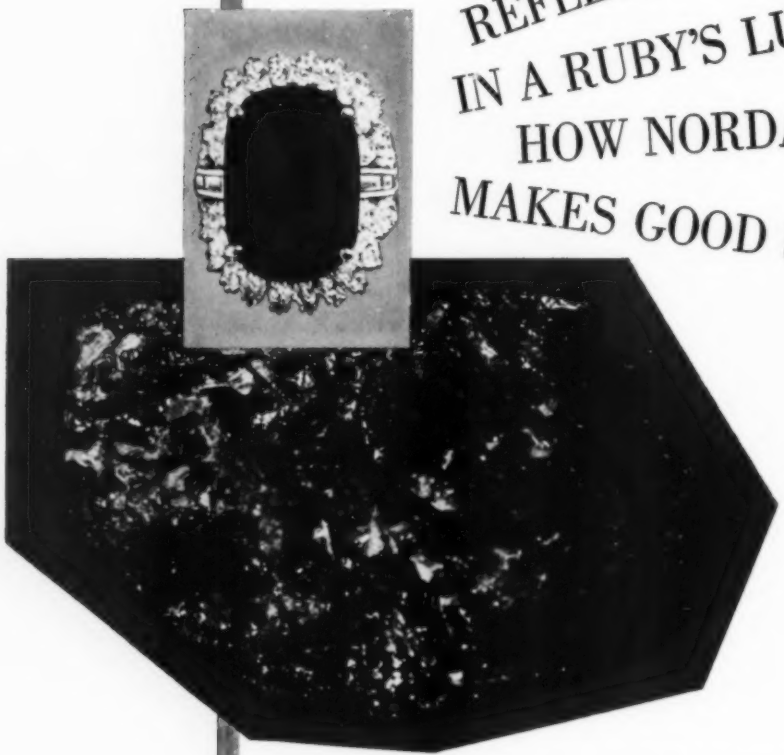
January, 1961

American Perfumer

REFLECTED IN A RUBY'S LUSTER..... HOW NORDA MAKES GOOD SCENTS



You can see a ruby is worth the trouble to make every facet true. People prize the flawless gem most of all.

Norda never forgets that when making scents for you. Each one that comes from Norda must be true, with never an imperfection, carefully shaped from the finest of Nature's materials.

Being a perfectionist has its rewards. Ask any Norda user.

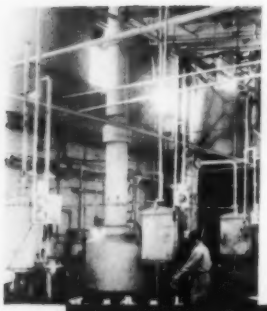
Norda®

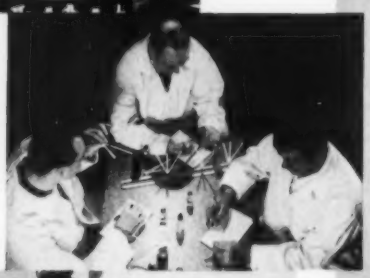
Norda makes good scents

Samples, free, by sending your business letterhead to
NORDA, 601 W. 26th St., New York 1, N. Y. • Chicago • Los Angeles • San Francisco • Toronto • Montreal • Havana • London • Paris • Grasse • Mexico City

duveen

DUVEEN SOAP CORPORATION
36-14 35th STREET • LONG ISLAND CITY 6, N. Y.
telephone: STillwell 4-7870





check first with Verley

for Combining Fragrance

TESTED ACCEPTANCE

to the best Advantage in your:

AEROSOL
COSMETIC
DETERGENT
INSECTICIDE
POLISH
SOAP
WAX

and many other specialized products.

Albert Verley & Company

1375 EAST LINDEN AVENUE, LINDEN, NEW JERSEY
1018 S. WABASH AVENUE, CHICAGO 5, ILLINOIS
21 EAST 40th STREET, NEW YORK 10, NEW YORK
McKESSON & ROBBINS, INC., Chemical Dept.
5353 JILLSON STREET, LOS ANGELES 22, CALIF.
AROMESCENCE INC.
10 RUE PERGOLESE, PARIS 16, FRANCE

• Synthetic Aromatic Products and Organic Intermediates • Bouquets and Finished Compositions
• Synthetic Flavoring Oils and Aromatic Bases • Essential Oils

American Perfumer

VOL. 76, NO. 1 JANUARY, 1961

Contents

Contenu
Contenido
Inhalt

DEPARTMENTS

Publishing Offices
418 North Austin Blvd.
Oak Park, Illinois
VIllage 8-6310

Eastern Office
358 Fifth Avenue
New York 1, New York
LOngacre 3-4382

P. W. Allured
Publisher

M. G. deNavarre
Editorial Director

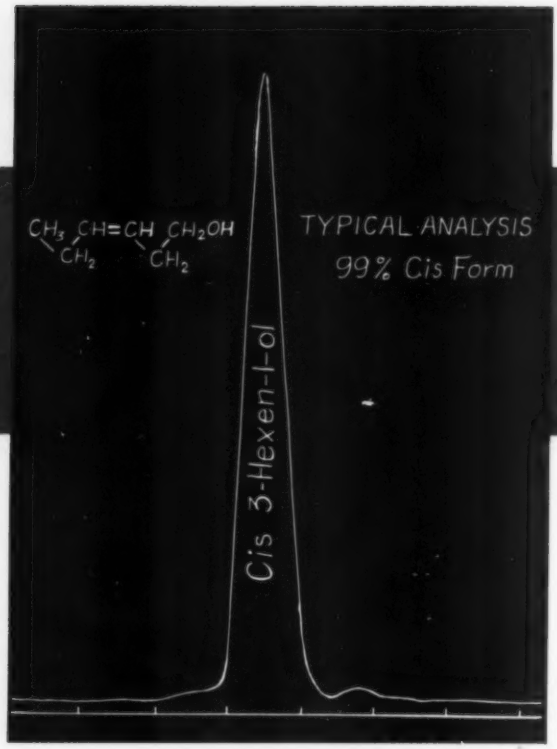
Stanley E. Allured
Assistant Publisher

John H. Muller
Eastern Manager

Mary Aslesen
Circulation Director

Janet Northrop
Advertising Production Mgr.

Published Monthly by Allured Publishing Corporation. Publication office: 1309 North Main Street, Pontiac, Illinois, U.S.A. Editorial and executive offices: 418 North Austin Boulevard, Oak Park, Illinois. P. W. Allured, President. Subscription Rates U.S.A., Possessions and Canada, $5 one year; $1.00 per copy. Other countries $15 one year. Second class postage paid at Pontiac, Illinois. Allured Publishing Corporation is also publisher of The Manufacturing Confectioner.



LEAF ALCOHOL

Now available, this unique alcohol of extreme purity, occurring widely in numerous plants, fruits and vegetables, and possessing the characteristic odor of freshly-cut foliage. Use traces of this leaf alcohol in your fine perfume and flavor formulations to achieve an ideal naturalness.

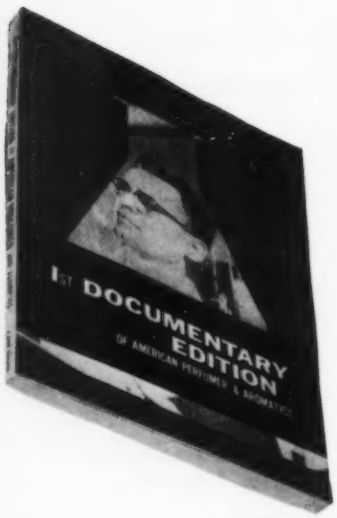
COMPAGNIE PARENTO INC.

CROTON-ON-HUDSON, NEW YORK

New York Office: 507 Fifth Avenue, Phone: MUrray Hill 7-5133

Compagnie Parento, Ltd. • 73 Adelaide Street West, Toronto 1, Ontario, Canada

ESSENTIAL OILS **PERFUME BASES**
AROMATIC CHEMICALS **FINE FLAVORS**



copies still available

1st Documentary Edition of American Perfumer

- formulations
- technical data
- processing techniques

Contents

ORDER TODAY **price $5.00**

American Perfumer
418 North Austin
Oak Park, Illinois

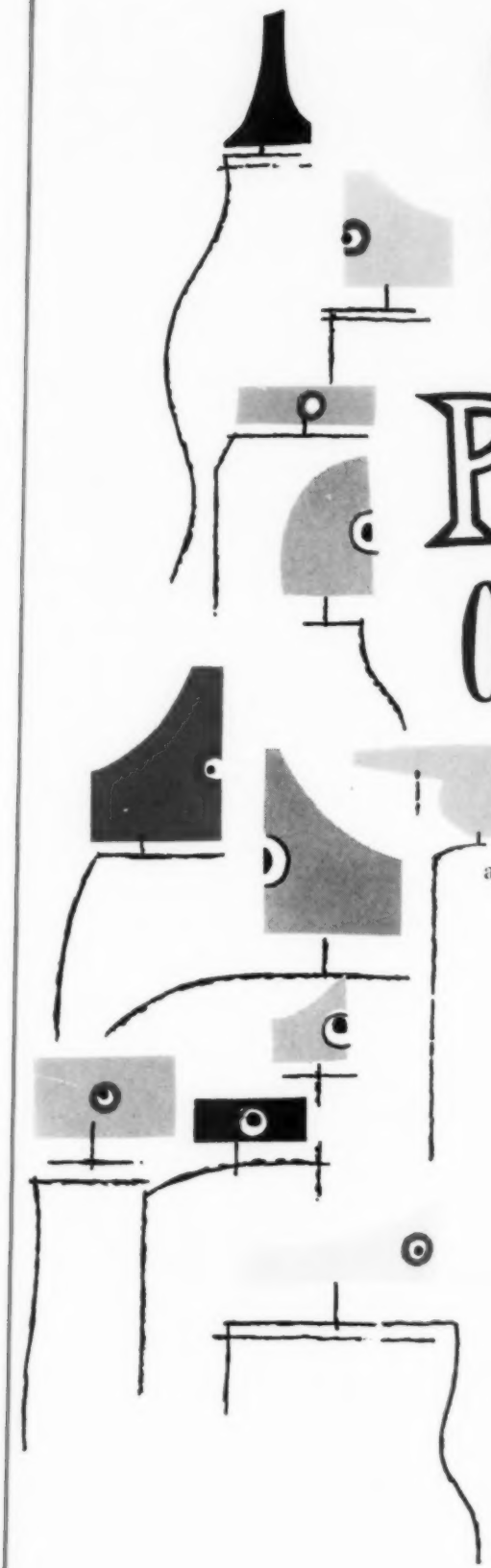
Please send me _____ copies of the 1st Documentary Edition (@ $5 per copy) for which I enclose _____.

Name_____ title_____

Company_____

Address_____

City_____ zone_____ State_____



Synfleur — when the PRESSURE'S on Fragrance

No mere adaptations or improvisations, Synfleur perfumes for aerosols are specially developed to meet the problems and challenges of aerosol dispensing and create repeat sales.

Synfleur perfumes for aerosols cover the entire range of spray products: cosmetics, shaving creams, pharmaceuticals, insecticides and repellents, air fresheners, colognes and perfumes, hair preparations, sachets, industrial products.

Close collaboration between expert perfumers and skilled aerosol technicians have produced the Synfleur aerosol perfumes to solve your scenting problems with current products or in the development of new ones.

Our seven decades of experience are at your service — ask for our technical assistance without obligation.

Synfleur
SCIENTIFIC LABORATORIES, INC.
MONTICELLO, N. Y.

ATLANTA • DETROIT • LOS ANGELES • NEW YORK • SAN FRANCISCO • MEXICO, D. F. • HAVANA • MONTREAL • Guatemala City • San Salvador • San Pedro Sula
Managua • San Jose • Panama • Barranquilla • Medellin • Bogota • Caracas • Maracaibo • Rio de Janeiro • Buenos Aires • Santiago

LANOLIN

ANHYDROUS USP X-TRA DEODORIZED GRADE
ANHYDROUS USP COSMETIC GRADE
ANHYDROUS USP PHARMACEUTICAL GRADE
ANHYDROUS USP INDUSTRIAL GRADE

DERIVATIVES

RITALAN (100% Pure Lanolin Oil). The lipid and oil soluble liquid lanolin—Hypo-Allergenic—Penetrant—Moisturizer—Plasticizer. Will not depress skin respiration.

RITACHOL (Liquid cholesterol emulsifier), Non-ionic—surface active—Hypo-Allergenic—Emollient—Moisturizer balanced free Cholesterol plus other Sterols.

ETHOXYLATED LANOLIN USP 50% & 100% Active. A water soluble hydrophillic lanolin with surface active properties.

FORLAN "T" A solid base containing active lanolin fractions to provide utmost emolliency and emulsion stability.

FORLAN "G" an inexpensive lanolin cholesterol base designed primarily for cream hair oils.

RITALATE Ethoxylated RITALAN. Designed primarily for hair products—rinses, shampoos, etc.

CUSTOM MADE LANOLIN DERIVATIVES EXCLUSIVELY DESIGNED FOR SPECIFIC CUSTOMER REQUIREMENTS

Write for suggested formulas and samples.

R.I.T.A. CHEMICAL CORP.

612 N. MICHIGAN AVENUE **CHICAGO 11, ILLINOIS**

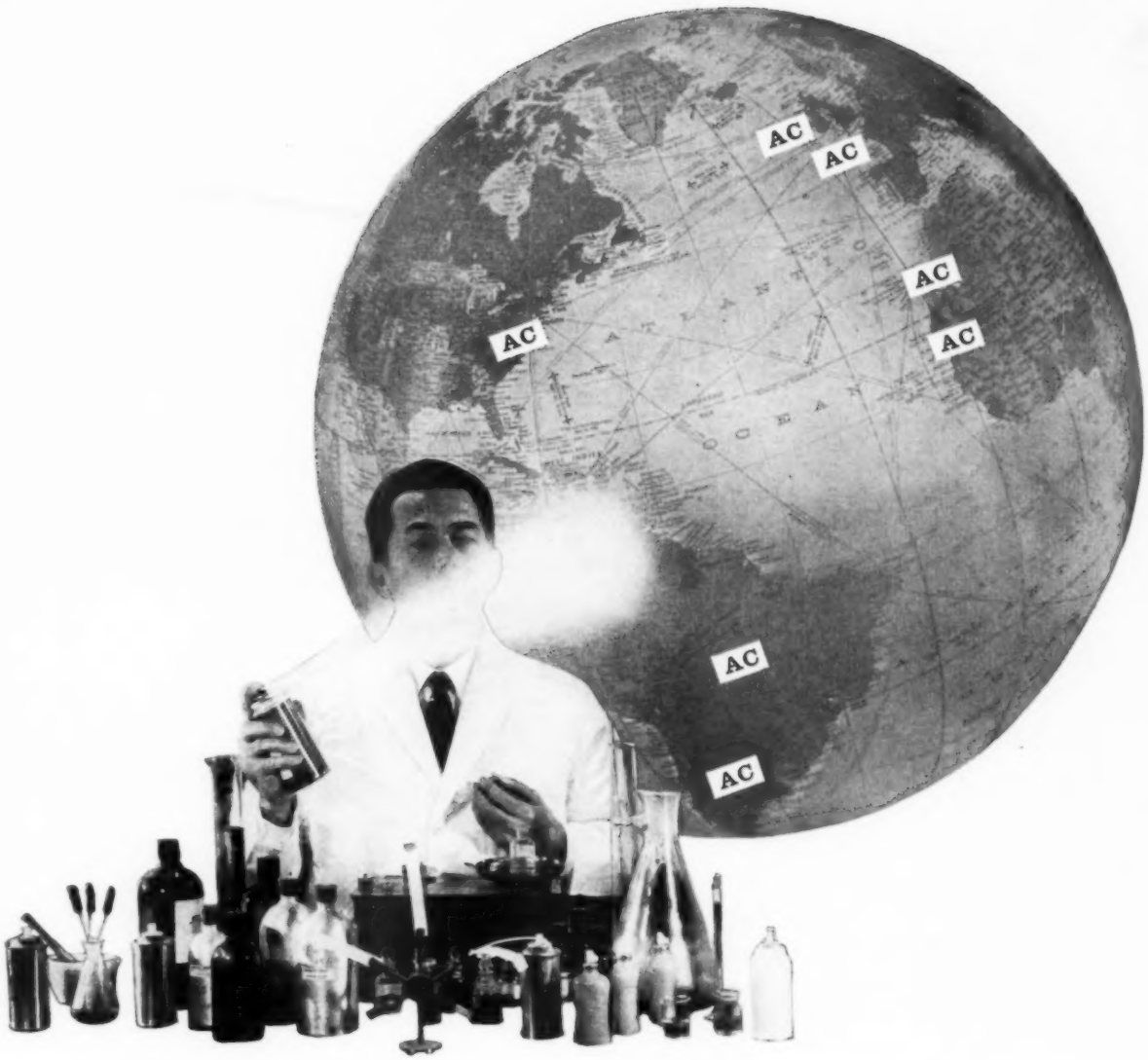
Telephone SUperior 7-0051

AGENTS

EAST COAST
J. L. SIMMONS CO.
10-11 46th Ave.
LONG ISLAND CITY 1, N. Y.
Phone: STILLWELL 4-3888

GULF STATES
L. H. BAILEY INC.
Balter Building
NEW ORLEANS 12, LA.
MAGNOLIA 2476

WEST COAST
G. L. GAMELCY CO.
440 Seaton St.
LOS ANGELES 13, CALIF.
MADISON 4-7927



Since 1768 the House of Chiris has dedicated itself to the Fifth Sense (Olfactive). In the development of Essential Oils, Floral Absolutes, Chemical Isolates, Synthetic Chemicals, and all those creations and specialties which combine industrial aromatics with natural products and produce fragrance, the House of Chiris has a cherished history. Today Chiris maintains laboratories headed by experienced chemists who have available to them not only the accumulated knowledge of generations of Chiris perfumers and chemists, but also the research facilities of six modern laboratories located in **Grasse and Paris, London, Sao Paulo (Brazil), Buenos Aires (Argentina), and New York City.** Whether Essential Oils, Isolates, or combinations thereof, are used as fragrance constituents by the perfumery, soap, cosmetics or allied industries, we are happy to be consulted.

ANTOINE CHIRIS CO., INC. 220 East 23 Street, New York 10, N. Y.

MANUFACTURING LABORATORIES
GRASSE • PARIS • LONDON • SAO PAULO • BUENOS AIRES
REPRESENTATIVES WORLD-WIDE

CITROPAL® contains the identical proportions of only those components which we found to be in terpene- and sesquiterpeneless natural lemon oil.

CITROPAL® combines the full pure odor and flavor with the stability, uniformity, availability, economy and other advantages of synthetic products.

CITROPAL® is particularly recommended:

a) In compounds for Perfumes and Colognes, all Lotions, Cosmetic Products, Soaps and Detergents.

b) In the manufacture of lemon-flavors.

DRAGOCO INC.

250 West Broadway, NEW YORK 13, N.Y.
Tél. Canal 6 - 58 13 15

CITROPAL®

A PERFECT REPRODUCTION OF TERPENELESS LEMON OIL

Note further details and suggestions from our data sheet.

Questions and Answers

Q. *I notice you often publish different cosmetic formulas in your publication which I imagine are current and tested. I would like to get a formula on eyeshadow, paste and stick, including the pearly type; how to make it and sources of material, as well as liquid waterproof mascara–stiffening type. K. F., N. J.*

A. As you know, we are not a consulting laboratory and we develop no products, whatsoever. All we can do in the way of formulations is to suggest the same which appear in the literature. Our recommendation to you is to obtain a copy of a cosmetic book, such as Sagarin's COSMETICS: SCIENCE AND TECHNOLOGY, which is available from the American Perfumer. Formula No. 205, given below, is taken from the CHEMISTRY AND MANUFACTURE OF COSMETICS, by deNavarre. It consists of:

Lanolin	10 parts
Spermeceti	13 parts
Petrolatum q.s.	100 parts

This formula is for the less oily type and in part the oiliness can be controlled by the melting point of the petrolatum. To this base, one adds from 8 to 12 per cent of color lakes depending upon the shade desired. We regret we cannot help you with liquid, waterproof mascara because these products are of very secret composition and not enough is known about them at this writing to make more than those suggestions which have appeared regularly in the American Perfumer, Question and Answer department which we are sure you have been reading. A source of pearl material for make-up has been sent to you by letter.

Q. *This may be out of your line but can you direct me to a source for the material used to apply to eye glasses to keep them from frosting or steaming in the winter? A. G., Minn.*

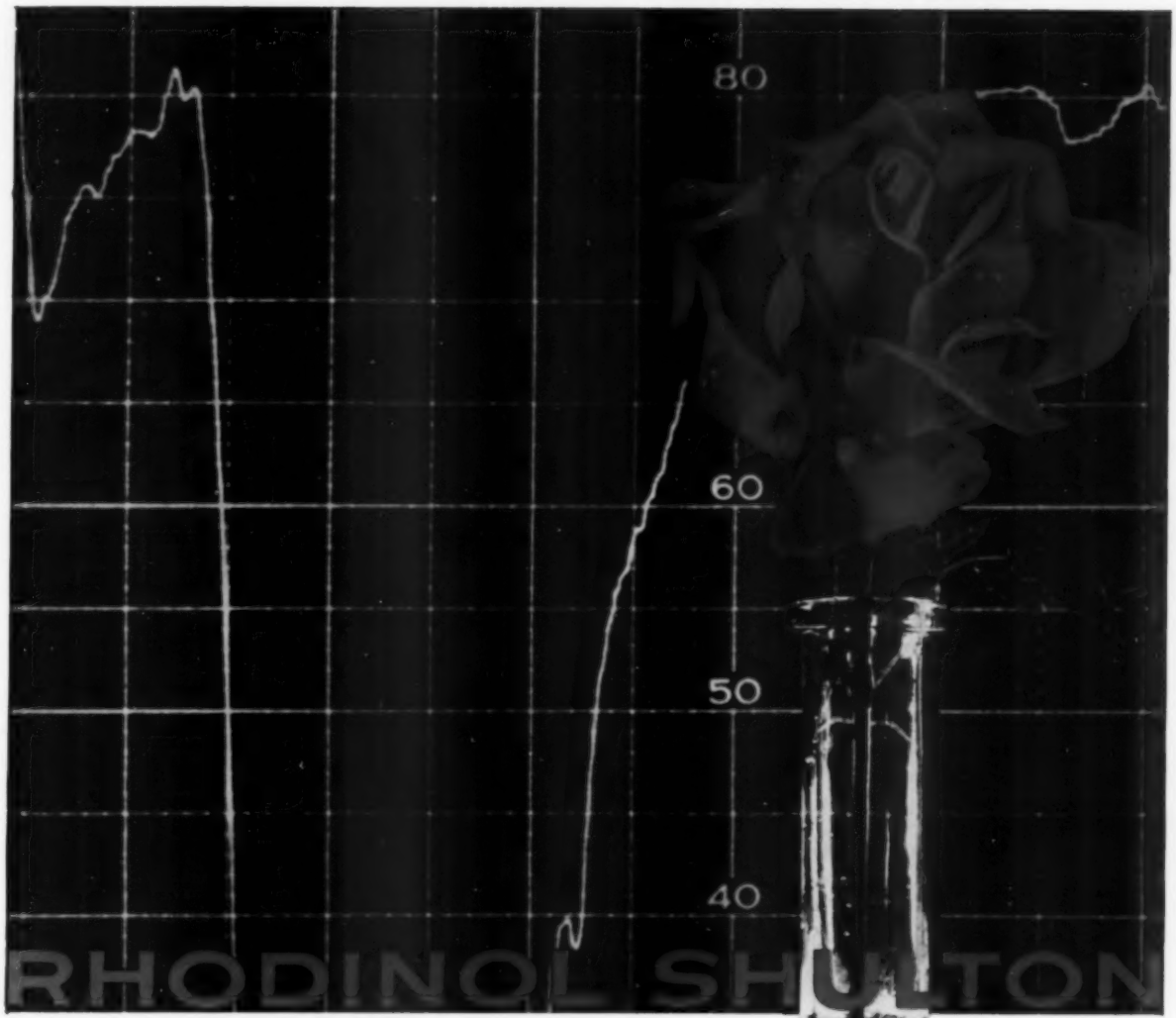
A. The solutions usually applied to eye glasses are alcoholic solutions of hard soap. This is applied and wiped dry. The remaining soap film prevents fogging.

Q. *The September, 1960, issue mentioned that there are at least three suppliers of dihydroxyacetone. Would you be good enough to tell just who they are? Also, must a royalty be paid to anyone if DHA is used in a sun tan lotion? The American Perfumer is one of the most informative trade papers–Ponce de Leon should have had a fountain like your "Desiderata." K. J., Texas*

A. Thank you for your kind observations regarding the American Perfumer and "Desiderata." The suppliers of dihydroxyacetone with whom we are acquainted are as follows: Charles Pfizer and Co., Inc. 630 Flushing Ave., Brooklyn 6, N. Y., Dawes Laboratories, Inc., 4800 S. Richmond St., Chicago 32, Ill., and Wallerstein Co., Wallerstein Sq., Mariners Harbor, Staten Island 3, N. Y. U. S. Patent No. 2,949,403, issued August 16, 1960, has been assigned to the owners of the "Man Tan" trademark. In using dihydroxyacetone you will be violating this patent and therefore subject to an infringement suit. It is our understanding that the Drug Research Corp., 369 Lexington Ave., New York 17, N. Y., are licensing companies under their patent to use DHA for the purpose of manufacturing skin tanning preparations.

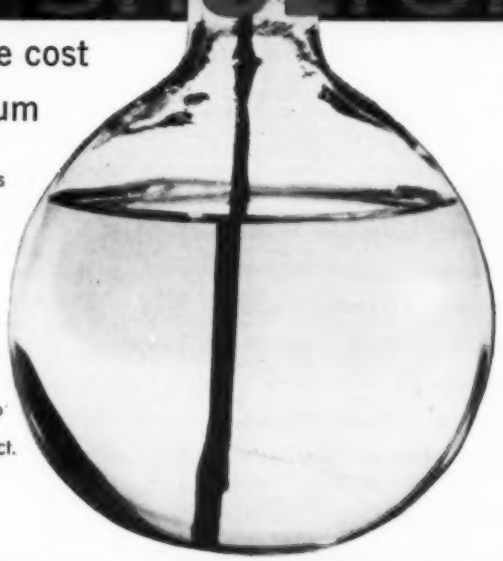
Q. *Will you be kind enough to supply us with the name of a manufacturer of a preparation called Keratine or similar adherent product. We would like to use this in our hair tonics and fingerwaving lotion. The preparation must be alcohol or water soluble. J. T. C., Va.*

A. Keratin is a substance of which hair is composed. Skin similarly is composed of keratin. There are products on the market that are keratin degradation mixtures, thus rendering the insoluble substance, water or alcohol soluble. One of these is called Vericrest. It is supplied by the Protean Chemical Corp., 150 Nassau St., New York 38, N. Y. We believe that if you write them you will get all the necessary information and suggestions for the adaption of their product to your particular usage.



superb rose effects at half the cost of rhodinol ex-geranium

Rhodinol Shulton is superior to ordinary rhodinols in its freshness effect . . . its blending power . . . its compatibility with the finest perfume materials . . . and its stability in soap. • Shulton's advanced research combined with the perfumer's artistry makes possible this rhodinol of finest quality and constant character. And you can rely on the quality of Rhodinol Shulton because it is free of impurities, free of batch-to-batch variations. • Specify Rhodinol Shulton to procure these superb rose effects at only half the cost you might expect.



SHULTON FINE CHEMICALS

DIVISION OF SHULTON, INC., 630 FIFTH AVE., NEW YORK 20, N. Y., CIRCLE 5-6263

Check List of Best Selling Technical Books

COSMETICS, SCIENCE AND TECHNOLOGY. The editorial board of this encyclopedia cosmetic work is made up of H. D. Goulden, E. G. Klarmann, and Edward Sagarin, executive editor. It is in five parts: I, Scope of Cosmetics (80 pages); II, Toilet Preparations (812 pages containing 800 formulas); III, Manufacture and Technology (214 pages); IV, Physiological Considerations (92 pages); plus preface and complete index. The sixty-five experts who contributed, are a "who's who" of cosmetic chemists in the United States and Canada. 1433 pages. Illustrated. Price $27.50.

HENLEY'S 20TH CENTURY BOOK OF FORMULAS, PROCESSES, TRADE SECRETS—REVISED, ENLARGED EDITION. Manufacturers, chemists and others call HENLEY'S the most valuable book of its kind. Nearly 10,000 formulas, processes, trade secrets. It contains formulas for nearly everything imaginable; new ways of doing things; technical process; so-called trade secrets. It has helped thousands make more from their present business and professions. A single formula may be worth more than 100 times the price of the book. Over 900 pages, completely indexed, cloth binding, $5.25 postpaid.

PRESSURIZED PACKAGING (AEROSOLS). By Alfred Herzka, Jack Pickthall. Although technical problems occur with all types of packages, those which arise with pressurized packages are many and complex. This reference book, by two recognized authorities deals with propellants, containers, valves, filling methods, laboratory procedures, emulsified systems, and perfumes. There is a complete section containing more than 200 formulations, including foods, insecticides, cosmetics, paints, and numerous other products. 400 pages. Illustrated. Price $12.00.

PERFUMERY SYNTHETICS AND ISOLATES. By Paul A. Bedoukian. This carefully compiled volume meets the genuine need for authoritative data on perfumery synthetics. It embraces the history, chemistry, physical and chemical properties, manufacture, uses, and other pertinent data of the principal perfumery compounds; and covers the important perfumery synthetics. A complete index adds to the value of this important work. 488 pages. Price $10.25.

THE HANDBOOK OF SOLVENTS. By Leopold Scheflan and Morris Jacobs. The most useful work of its kind today. Part I covers theoretical aspects and practical attributes such as solvent action, solvent power, evaporation and evaporation rates. In Part II the physical constants of over 2700 liquid compounds are tabulated for easy comparison. 728 pages. Illustrated. Price $12.00.

COSMETICS—THEIR PRINCIPLES AND PRACTICES. By Ralph G. Harry, discussed the skin, its nutrition and scientific care: the hair, its proper grooming, the physio-chemical problems involved in its washing; the teeth and their care, covering the present status of different dentrifices, and the luster-producing properties of ingredients. Much of the information has its source in the research activities of its author, embracing chemistry, dermatology, and microbiology. 786 pages. Illustrated. Price $17.25.

INTERNATIONAL ENCYCLOPEDIA OF COSMETIC MATERIAL TRADE NAMES. By Maison G. deNavarre, brings you reference data you will turn to constantly . . . the most complete listing of all the materials of the world used in cosmetic manufacture . . . including quick concise descriptions of approximately 4,000 materials . . . the names and addresses of the suppliers . . . and a very useful cross-index of the materials and their uses. You will use it when seeking new materials, or substitutes for those you may now be using. 400 pages. Price $7.50.

HANDBOOK OF COSMETIC MATERIALS. (Their Properties, Uses and Toxic and Dermatologic Actions). By Leon Greenburg and David Lester. Contains alphabetical listing, with frequent cross references, of information on approximately 1,000 substances. For each compound gives: formula (including collateral names), properties, toxic action, dermatological action. Exhaustive bibliography. Essential for manufacturing chemists cosmetic industry, dermatologists, allergists. 467 pages. Price $13.50.

THE ESSENTIAL OILS. By Ernest Guenther, with the collaboration of leading experts, this monumental six-volume work includes: Vol. I, Origin and Development of Essential Oils. 427 pages. Price $9.50. Vol. II, detailed data on several hundred constituents of essential oils. 852 pages. Price $13.50. Vol. III, discusses the oils of the plant families Rutaceae and Labiate. 777 pages. Price $13.50. Vol. IV, covers the widely used oils: citronella, lemongrass, bois de rose, cassia, and others. 752 pages. Price $13.50. Vol. V, takes up other oils of special interest to flavor, perfume and soap manufacturers: rose, ginger, cardamon, anise. 507 pages. Price $13.50. Vol. VI, completes the monographs on individual oils: wintergreen, sweet birch, juniper berries, and the numerous pine oils. 552 pages. Price $13.50.

MANUAL FOR THE ESSENCE INDUSTRY. By Erich Walter. Comprises methods, with formulas for making all kinds of essences for liquors and alcoholic drinks, fruit juices and jams, mineral waters, essences for fruits and other vegetables, essences for confectionery and pastry. Describes raw materials and laboratory practice. Discusses taste and the transfer to foods and beverages. 427 pages. Illustrated. Price $8.25. Published 1916.

AMERICAN PERFUMER DOCUMENTARY

Now, between the covers of the new AMERICAN PERFUMER DOCUMENTARY, you can have a wealth of current information . . . formulations, technical data, and processing techniques for . . .

- **HOUSEHOLD SPECIALTIES**
- **PHARMACEUTICAL COSMETICS**
- **PRESERVATIVES & ANTI-OXIDANTS**
- **SURFACTANTS**
- **COSMETIC EMULSIONS**
- **AEROSOL PACKAGING**

Whether you are a research director, chemist, or technician, you will want to have this important reference work always handy in your working library.

Price $5.00 postpaid

- ☐ **COSMETICS, SCIENCE AND TECHNOLOGY. — $27.50**
- ☐ **HENLEY'S 20TH CENTURY BOOK OF FORMULAS. — $5.25**
- ☐ **PRESSURIZED PACKAGING (AEROSOLS). — $12.00**
- ☐ **PERFUMERY SYNTHETICS AND ISOLATES. — $10.25**
- ☐ **THE HANDBOOK OF SOLVENTS. — $12.00**
- ☐ **COSMETICS—THEIR PRINCIPLES AND PRACTICES. — $17.25**
- ☐ **INTERNATIONAL ENCYCLOPEDIA OF COSMETIC MATERIAL TRADE NAMES. — $7.50**
- ☐ **HANDBOOK OF COSMETIC MATERIALS. — $13.50**
- ☐ **THE ESSENTIAL OILS. (Specify Volume)**
- ☐ **MANUAL FOR THE ESSENCE INDUSTRY. — $8.25**
- ☐ AMERICAN PERFUMER DOCUMENTARY. — $5.00

AMERICAN PERFUMER, *Book Dept.*

418 N. Austin Blvd., Oak Park, Illinois

Enclosed find check for $ for which send me the books checked.

Name .....

ADDRESS ☐ **Home** ☐ **Business** .....

City ..... **Z** ..... **State** .....

Company .....

DESIDERATA

Maison G. deNavarre, M.S., F.A.I.C.

Who Is Miss A. D. Stabile?

The November (U.S.A.) and December (Canada) Readers Digest carries an article entitled "The Outrageous Cost of Facial Beauty" or "Beware of *Costly* Magic Aids to Facial Beauty", (my ital.) over the name of this author. Readers Digest seems to know little about her.

It has created a little stir among women cosmetic users. The story is typical of this type of presentation. Shades of "Skin Deep"!

Certainly the language is purposely used to give a particular impression. Some of the "facts" as this reader knows them are not *exactly* so. For example, to my knowledge, F.D.A. has required the hormone content to appear on labels all along, not just since 1951. Furthermore, in my years of contact with the industry a pricing formula for all products is used—not what the traffic will bear. There are a few who may not be so ethical, but we have these people in all walks of life, writers included.

If it weren't for royal jelly and placenta the author wouldn't have much to write about. And here, I repeat, the fact that lack of usefulness to skin of either substance has NOT been proved. Personally, I don't buy what has been said about these ingredients in consumer advertising but by the same token no scientific effort has been made to show them worthless. Only the poor scientific literature has been criticized. For my part, until someone shows usefulness for royal jelly to man, I am on the dubious side—but only a fool would say there isn't any.

On Placenta, maybe the facts will come to light more quickly. We need more facts—some of which are undoubtedly in the hands of research departments of the industry but are being withheld.

If Miss Stabile wants to make an issue of profits let her analyse the profits of the cosmetic manufacturers and compare them to the drug or other industries. She keeps forgetting the labor, overhead, cost of doing business, fringe benefits to labor and related items. I don't think our profit picture as an industry needs any apology. If she wants to pick on a couple of manufacturers lets slant the story that way, not use them as typical of the industry.

Notes

A new German product called Pollycenta contains placenta extract, turle oil, wheat germ oil, corn germ oil, vitamins, chlorophyll, lecithin, phytosterol and histidine. It is intended to reactivate all layers of the skin, strengthen tissue and correct wrinkles. . . . . The German Goldschmidt organization have patented (German #1,045,-601) the use of certain ampholytes such as 3-dodecyl-oxypropylaminobutyric acid in germicidal shampoos. . . . . By the way, Glyco Iberia has no connection with the U. S. company of the same name (at this writing). . . . . Looks like solidified polyol gel lipsticks are trying for a comeback. . . . . De Kay and Banker recently published (J.A.-Ph.A., *49*, 75, 1960) an interesting comparison of emulsifying equipment. . . . . Guess has made a study (J.A.Ph.A., *49*, 736, 1960) of the HLB of tragacanth gum. He raises the point—"it would be interesting to determine if tragacanth has an HLB in the true sense as do synthetic surfactants." He thinks it is an apparent value only. . . . . A provisional list of Cosmetic Colors has just been published in Germany as a book (Franz Steiner Verlag G.m.b.H., Wiesbaden Bahnhofstrasse 39, Germany). . . . . Heard a number of new approaches to effective personnel management at

the mid-year General meeting of the Canadian Toilet Goods Manufacturers Association in December. Address was given by Dr. J. C. Sawatsky, Assoc. Prof., School of Business at the U. of Toronto. . . . . X-irradiation of essential oils causes only a slight increase in antifungal properties. . . . . Hydroxypropylmethyl cellulose is permitted in foods for certain purposes and in specified amounts. . . . . The enzyme Peroxidase enhances ageing brandy. So does the use of ultrasonics. . . . . According to a study by Finholt, emulsified fats don't oxidize any more readily than straight fats (Pharm. Oct. 6, Helv. 35,333 (1960).

Advertising Expenditures

In a survey of advertising expenditures, Television Magazine gives totals for twelve companies spent in the 10 year period. General Motors has spent almost 825 million dollars. Second largest is P & G, approximately 732 million. Of the twelve companies, four have substantial interests in the toilet goods field. Lowest spender was General Mills, only 230 million. Revlon, who aren't listed in the twelve, spent 944 thousand in 1950 and over 12 million in 1959.

Little wonder a person intending to be a newcomer in the industry gets cold feet. Yet industry has a crying need for newcomers, the backbone of any progressive society. How can it be done?

DIE ATHERISCHEN OLE, Vol. III A, E. Gildemeister/Fr. Hoffman, revised by W. Treibs and D. Merkel, Akademie Verlag, Leipziger Str. 3-4, Berlin W.1, Germany. 1960. 628 pages. Price DM 63.00 (Approx. $16.00).

This volume is devoted to the discussion of hydrocarbons and the alcohols.

The hydrocarbons include chapters on aliphatics, polyprenes, aromatic and unclassified compounds. The alcohols include aliphatic and the polyrenes.

In the discussion of terpenes, the monoterpenoids are divided into acyclic, monocyclic, bicyclic, tricyclic and the sesquiterpenes. The alcohols include the saturated and unsaturated aliphatics and the monoterpene alcohols.

It was interesting to find three pages devoted to the monocyclic sesquiterpene hydrocarbon Bisabolen. This terpene is found in numerous essential oils among them the conifer oils, Petitgrain, lavandin, opopanox and sandalwood. (It has recently been patented as a perfume fixative).

The section on azulenes is similarly well done. It is good to see the fine work such as that of Haagen-Smit, Ruzicka, Sorin, Herout, Naves, Watanabe, Simmons and others so well reviewed.

The literature is heavy in pre-1939 material but does include a great many references through 1956.

It is not just a book on organic chemistry. The subject is treated as if it dealt with perfumery standards. Indeed the monographs have all the appearance of a pharmacopoeia with extensive references. Add this volume to the others on the same shelf with Guenther's ESSENTIAL OILS and you have a truly great reference set.

Volume V, edited by W. Triebs and K. Bournot. 1959, 766 pages, Price DM 60.00 (Approx. $15.25).

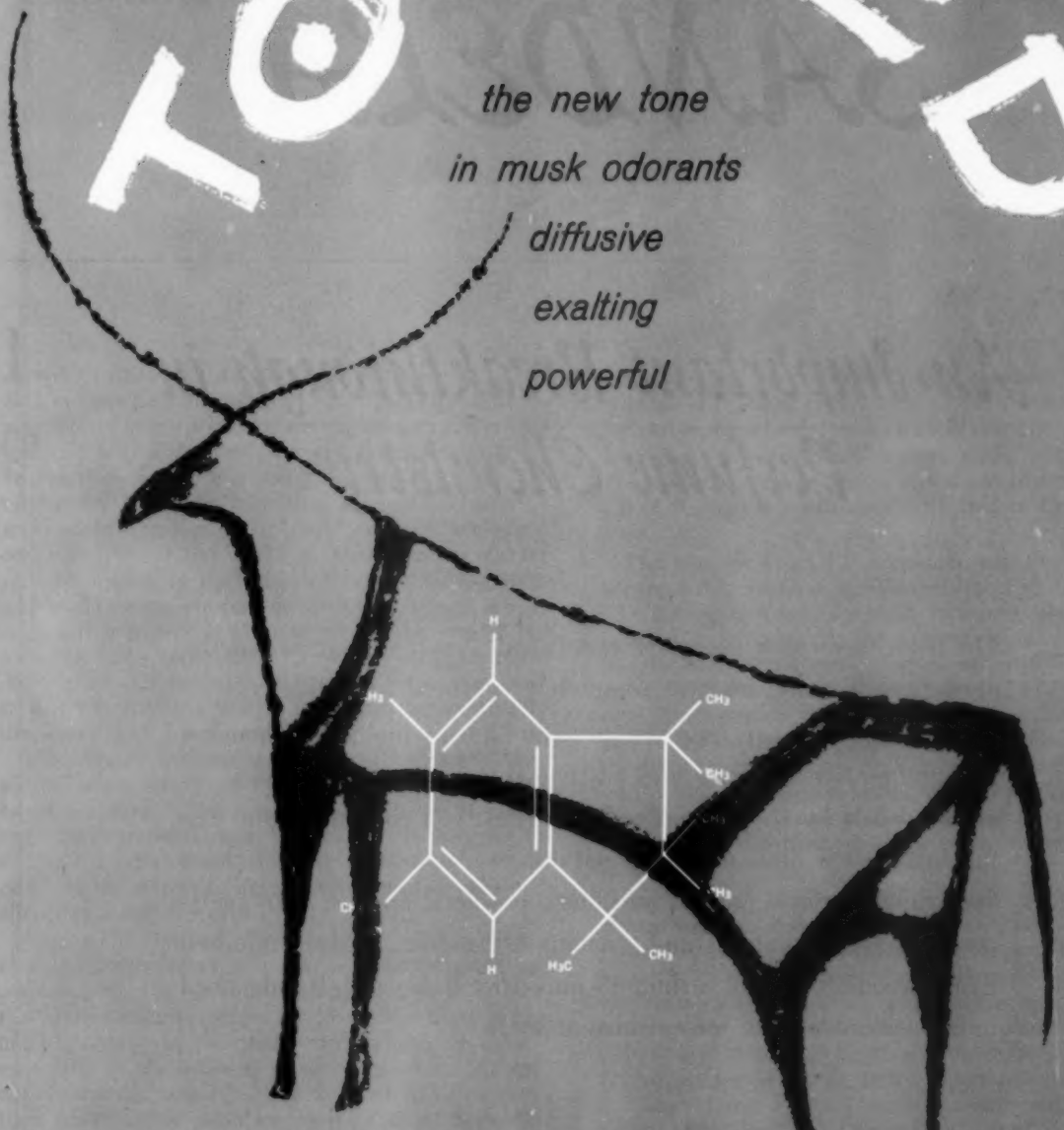
This volume consists of a series of monographs on essential oils derived from various plant families starting with the Lauraceae and ending with the Vitaceae.

It is regretable that no work has been reported on the orange flower water oil since 1938. In fact there are only a few references since the late war on important oils, such as neroli Bigarade, linaloe, Ceylon cinnamon and cassia. Rose oil fares a little better. Of course, in some cases there has been no new work done as with Reseda. But one gets the feeling that the coverage is not as good as Guenther, although including some later references and data.

However, each volume cannot be of equal quality although it is in the hands of at least one continuing author in this vast series. Even so, it is an important reference work.—(M. G. deN.)

TONALID

the new tone
in musk odorants
diffusive
exalting
powerful



PFW

FRUTAL WORKS: MIDDLETOWN, N. Y. • AMERSFOORT, HOLLAND • BREMEN, GERMANY • BRUSSELS, BELGIUM • MANIZALES, COLOMBIA • SOFLOR LTD.-PERIVALE, ENGLAND

The active principles of plants in cosmetology

H. Janistyn

In our restless age, in which the environment of the skin is becoming increasingly unnatural, the skin reacts with a stress whose many causes can seldom be influenced by a cosmetic, however good this may be. In response to the increasing inimicality of the environment, so-called "biological cosmetic science" is seeking, by the use of naturally existing "biological complexes" from the world of plants, to prevent or reduce damage to the skin, without subjecting it to additional strains imposed by unnatural substances. It is true that in this connection some members of the industry have committed speculative exaggerations. An important function is played by empiricism, and it does not appear that this factor can be completely dispensed with for the time being.

The idea of employing "biological vegetable complexes" is not new, but doubtless interesting. It also has disadvantages, because the constituents of plants are subject to fluctuation. Moreover, it is incorrect to equate the internal effect of herbs with their external effect on the skin or to draw conclusions from the one effect regarding the other.

Among the "biological principles" of plants particular recommendation is made in advertisements for cosmetics by the vitamins and hormones. It is true that some vitamins can be absorbed, but there is not much purpose in discussing this subject in detail, especially as the majority of tests have been carried out on animals, which have a different skin structure. It is questionable whether vitamins applied to the skin have a direct effect on the skin cells, though the possibility that some vitamins have an effect on the skin should by no means be rejected. To some extent the vitamins develop a specific effect on the skin which is often not identical with the actual vitamin effect. Many substances behave similarly, e.g. salicylic acid, which to some extent develops other functions when applied externally than when taken internally. It may be assumed that in this respect vegetable substances may be highly similar. For a number of years a complex of certain vegetable active principles has been termed "phytohormones" or "biostimulants". These expressions cover a multitude of vegetable ingredients, such as bioflavonoids, vitamins, hormones, organic acids, amino acids, sugars, etc.

At present we are not in a position to equate the effect of vegetable estrogens with that of the animal ones.

The genuine vegetable hormones, e.g. the auxines, are probably without significance for the organism. (2) Estrogens of the steroid type are also found in the vegetable world, but in many cases the compounds have a different composition with an estrogenic character. Butenandt and Jacobi (3) have found estriol or estrone in the catkins of willow trees and in the residues of palm kernels. Significant fertility disturbances occasionally occur in grazing animals which consume large amounts of fresh plants, just as individual disturbances can be caused by plants in humans (e.g. disturbances of the cycle in women hop-pickers).

According to Bradbury and White (4) at least 60 plants with an estrogenic effect are known today. Principles resembling cortisone also appear to occur naturally in several plants. Better known in this connection is radix Liquiritiae, whose action was already mentioned by Dioscurides (5). Among plants particularly rich in estrogenic substances are Allium sativum L., Arrhenaterum elatius, Butea superba Roxb., Elaeis guineenis Jacq., Festuca rubra, Lolium multiflorum, Salvia officinalis L., Taraxacum off., and Zea mays (green plant) (6).

It is a familiar fact that the estrogenic effect is not restricted to the four ring system of the steriod skeleton alone. For example, naphthalene derivatives, such as diphenyl-α-naphthylcarbinol and 1-keto-1, 2, 3, 4-tetra-hydrophenanthrene, have also proved to be active. Phenyl-substituted ethane derivatives are active and some stilbenes (stilboestrol, hexoestrol) are particularly active. The latter are fully active when two OH groups are present in the 4,4′ position. The stil-

benes of the vegetable world deviate from this chemical structure and have long been known as plant ingredients, e.g. rhaponticin in Rheum rhaponticum. The starting material in the synthesis is probably anol. Many plants contain stilbene derivatives, e.g. Pinus and Chlorophora excelsa (chlorophorin). The heart-wood of Pinus contains 3,5-dioxystilbene (pinosylvin), pinosylvin monomethylether, and various flavones and flavonones. Pinosylvin and rhaponticin do not have the characteristic 4,4′ OH link and their activity is therefore slight. Nevertheless, when administered in an amount of 0.6 mg., rhaponticin, which has been clinically tested by Probst, leads to a positive vaginal smear (7). The stilbenes are probably the most important carriers of the estrogenic properties of peat, bitumen, brown coal, tar, and petroleum.

A very widely distributed group with a partial estrogenic effect comprises the isoflavones (bioflavonoids). Attention was first drawn to this effect by the mass fertility disturbances which affected grazing animals (sheep) in southern Australia in 1939-40. In 1952 Curnow and Bennets (8) succeeded in tracing the sterility to genistein (5,7′-trihydroxyisoflavone), which is a component of Trifolium subterraneum (Dwalganup). Rosaceae, many Leguminosae, and also Sophora japonica contain isoflavone derivatives too. It is true that, compared with the activity of the steroids, the effect (weight against weight) is slight. An exception is formed by the estrogen of the Siamese legume Butea superba, whcih does not belong to the steroids. In Siam the tuber of Butea is used as an aphrodisiac. When taken orally the active principle is 60 to 70 times as potent as the hormones of the body itself. According to Butenandt and Jacobi (3) its exact composition is not known.

Some plants containing isoflavones

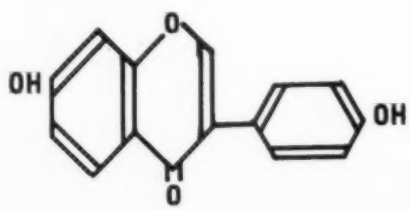
Name	Family	Compound
Cicer arietinum L	Leg.	biochanin A (genistein-4′-methyl ether)
Ferreires spectabilis	Leg.	biochanin A
Genista tinctoria L.	Leg.	genistin (genistein-7-glucoside)
Prunus sp.	Ros.	prunetin-glucoside
Prunus puddum	Ros.	prunetin
Pterocarpus angolensis	Leg.	prunetin
Sophora japonica L.	Leg.	sophoricoside (genistein-4′-glucoside) sophorabioside (genistein-4′-1-rhamno-d-glucoside)
Soja hispida	Leg.	genistin
Trifolium subterraneum L.	Gentian.	5,7,4′-trihydroxyisoflavone (genistein as a glucoside) biochanin A ononetin (2,4-dihydroxyphenyl-p-methoxybenzylketone)

Soya oil contains 7,4′-dihydroxyisoflavone (deidzein) and Meliiotus incar. contains 5,7-dihydroxy-4′-methoxyisoflavone(biochanin A). Formononetin (7-hydroxy-4′-methoxyisoflavone) is said to be inactive. Ladino clover contains a number of estrogenic substances, cumestrol genistein (and a new one $C_{15}H^8O^5$, not an isoflavone). The structure to the right is attributed to genistein.

It is absolutely certain that many plants promote or impede the hormonal functions of the organism (fertility, sexual cycle, lactation etc.). Extracts from Lithosperum ruderale reduce the fertility of experimental animals (10), and the same applies to Caladium seguinum. According to Lins (11) Vitex agnus castus has an effect resembling that of progesterone, which, however, is exercised through suppression of the gonadotrophic functions of the anterior parts of the hypophysis. H a n s e l (12) isolated a glucoside which was recognized as the p-hydroxybenzoic acid ester of aucubin. The highly active ingredients of hops have also been tested for their estrogenic effect. Zenisek (13) was able to show that the so-called β-acid in hops has a relatively powerful effect.

However, not only the vitamins and estrogens are receiving the attention of cosmetic science. Numerous other ingredients of plants are said to have cosmetic properties. The cosmetic effect is attributed primarily to the tannins, essential oils, dyestuffs, pro-azulenes, bitter principles, silicic acid compounds, fruit acids, coumarin derivatives etc. Cosmetic properties are also possessed by the germ oils rich in essential glycerides (wheat, maize), extracts from cereal germs, brans etc. The vegetable materials stated to have been treated by Filatow's methods and concerning which very vague information is available require closer examination.

Very important also are plants containing coumarin derivatives; all of them are of high pharmacological activity (14). Among these are the simply constituted coumarins aesculin, fraxin, osthrutin, umbelliferone, herniarin, scopoline, daphnin, fraxinol, osthol, and osthneol, as well as the furan coumarins with a 2,2′-dimethyl-1,2-chromic ring, such as angelicin, psoralen, bergapten, xanthotoxin, pimpinellin, imperatorin, ostruthol, oreosolon, peucedanin, nodakenin, etc. A phototropic isomeric diradical forms under the influence of ultraviolet light. By means of a further O-atom the resulting quantum-mechanical excitation of the C-atom permits a peroxydic oxygen link, which easily transfers the oxygen, at the quinoid group. (15) This applies particularly to hypericin and its preliminary forms. Extracts from Hypericum perforatum are becoming used to an increasing extent in cosmetic science and have a good effect. (16) This plant also contains essential oil and quercetin, partly in the form of a galactoside. Angelica archangelica and likewise Peucedanum osthrutium and Pimpinella saxifraga are particularly rich in coumarin derivatives. When taken internally all these herbs lead to a feeling of bodily wellbeing, mental harmony, and a general improvement of efficiency. Good service is rendered by baths with Angelica. It is possible that the bioflavonoids mentioned likewise improve the bodily functions in another way and thus exercise indirectly an estrogenic function too (pro-estrogens). A list of the most important plants at present recommended for cosmetics will clarify the picture. A rigid table cannot be given because the active principles often overlap:



1. *Plants and parts of plants with a tanning effect (tannins):*
   Arnica montana, Euphrasia, Rhiz. Rhei, Sambucus nigra, Rad. Bardanae, Flor. Tiliae, Melissa off., Thymus serpyllum, Rosmarinus off., Salvia off., Achillea millefolium, Viola tricolor, Thymus vulgaris, Potentilla silvestris, Juniperus communis, Salix nigra, Crataegus Hamamelis virginiana, Cort. Chinae, Myrtus communis, Taraxacum off., Tussilago farfara, Veronica, Ruta gravioles.
2. *Plants in which essential oils, among other substances, are active:*
   Arnica montana, Foeniculum vulgare, Pinus silvestris, Lavandula off., Thymus serpyllum, Rosmarinus off., Thymus vulgaris, Laurus nobilis, Melissa off., Mentha piperita, Populus nigra, Achillea millefolium (chamazulene), Matricaria chamomilla, Humulus lupulus, blossom lotions (rose, orange, elderberry, lavender, ylang-ylang, Salvia sclarea etc.)
3. *Plants which, among other substances, contain histamine, acetyl choline etc.:*
   Urtica dioica (Urt. urens), Calendula off., Sambucus nigra, pollens.
4. *Plants which, among other substances, contain glucosides, saponins, alkaloids etc.:*
   Urtica dioica, Cort. Chinae, Flor. Tiliae, Petroselium sativum, Agropyrum repens, Cort. Quillaiae, Sem. Hippostani, Salvia off., Viola tricolor., Thymus vulgaris, Juniperus communis, Crataegus, Fol. Jaborandi (Pilocarpus pennatifolius), Gentiana lutea.
5. *Plants containing carotinoids among other substances:*
   Hypericum perforatum, carrot.

Further ingredients are pectins, mucins, sulphur, trace elements, and enzymes. The last-mentioned will seldom remain stable, however. The active principles and ingredients determined by various methods are usually quoted as being present in all parts of the plant, but this is not always true. For example, birch bark extracts and birch lotion contain no betuline, about whose action, incidentally, nothing is known.

The plants are used primarily in the form of tinctures, but also as decoctions and other extracts, and are recommended for creams of every description, face lotions, hair lotions, face packs, bath additives etc. Depending on their nature, astringent, tonicizing, anti-irritant, and hair growth-promoting influences, and favourable influences on dirty and greasy or dry skin are attributed to them. To some extent they have been claimed to influence skin atrophy, but this has, of course, not been proved. Pollen extracts, which not only contain vitamins, but also hormones, amino acids, and unknown substances too, are frequently recommended. The advertisements are ahead of the effects actually achieved.

A thorough knowledge of the ingredients of plants, and likewise their standardization, are important prerequisites for their use. Only then can they be suitably and economically employed.

An extract from de-oiled wheat germs**, which has been shown by the clinical test to have an estrogenic action, will serve as an example. Among other things, the presence of numerous amino acids, sugars, and bioflavonoids has been established. The presence of steroidal estrogens could not be proved by chromatography, but it is possible that the amounts are too small or that other active compounds are present.

Thus the presence of several active substances to which, according to the present state of knowledge, a favourable effect can be attributed, is proved (amino acids, glucose, rutin). It would be a good thing if all extracts etc. were tested in the same way.

Summary:

In cosmetic science on the continent a desire has become visible to employ "biological vegetable complexes"; it is believed that this makes it possible, without subjecting the skin to the strain imposed by unnatural substances, to produce preparations with a nuturing and curative or preventive effect. Many recommended plants are ones used in folk-medicine and their effect must be more carefully examined. However, the suggestions cannot be ignored, for the cosmetic effect of many substances of vegetable origin is unmistakable. An example is an extract of de-oiled wheat germ, which has been tested by the author. It must also be taken into account that even sub-threshold amounts of the active principles have a cumulative action and can lead to a favourable effect.

References

1) Luders-Lohde, Chr.: Kosmetik als Mittel der Gesundheitserziehung Fette, Seifen, Anstrichmittel **60**, 389(1958); **60**, 1067(1958). Parfumerie u.Kosmetik **40**, 666(1959)
2) Leuthardt F.: Lehrbuch der Physiologischen Chemie, 13th edition, 671 usw.
3) Butenandt A. und Jacobin H.: Uber die Darstellung eines kristallisierten pflanzlichen Tokokynins (The likinins) und seine Identifiezierung mit dem α-Folikelhormon. Zschr.f.Physiol. Chem. **218**, 104-112(1933)
Dohrn M, Faure W., Poll H. und Blotevogel W.: Tokokinine, Stoffe mit Sexualhormonartiger Wirkung aus Pflanzenzellen. Med. Klin. **22**, 1417 1419 (1926)
Koch W. und Heim G.: Die Speicherung von Oestrogenen im Tierkorper. Endokrinologie, **30**, 335-338(1953)
Loewe S. und Sporr-Dorpat E.: N chweis und Gehaltsbestimmung des weiblichen Brunsthormones in weiblichen Organen des Pflanzenreiches. Ann. Akad. Wiss., Wien **63**, 167 (1926)
Loewe S., Nance F. und Spohr E.: N Uber weibliche Sexualhormone (Thelytropine) brunsterzeugende Stoffe (The lykenine) als Erzeugnisse des Pflanzenreiches. Biochem. Ztschr. **180**, 1-26 (1927)
Pieterse P. J. S. und Andrews F. N.: The estrogenic activity of legume, grass and corn silage. J. Dairy Science **39**, 80-89 (1956)
Thiers H, Zwingelstein G. und Jouanneteau J.: De l'emploi therapeutique d'une solution das l'alcool ethylique de l'insaponifiable de l'huile rouge de palme. Lyon Medical (1955), 221-223.
Vauge J:, Garrigues J. C., Berthet J. und Favier G.: Note sur l'action oestrogene de divers corps gras. Ann. D'Endocrinologie (1957) 745-751.
4) Bradbury R. B. und White D. E.: Vitamins and Hormons **12**, 207 (1954)
5) Hansel R.: Einige neue Ergebnisse der Arzneipflanzen-Forschung Deutsch. Apoth. Ztg. **41**, 1037-1042(1959)
6) Orzechowski G.: Uber gonadomimetische und gonadotrope Wirkstoffe in Pflanzen. Pharm. Rundschau **1**, 1-7(1959)
7) ibid.
8) Curnow D. H. und Mitarb.: Australian J. exptl. Biol. Med. Sci. **26**, 171(1948)
Curnow D. H.: Biochemic. J. **58**, 283(1950)
9) Hansel R.: Einige neue Ergebnisse der Arzneipflanzen-Forschung Deutsch. Apoth. Ztg. Nr. 41, 1037-1042(1959)
10) ibid.
11) ibid.
12) ibid.
13) Zenisek Anton: Beitrag zur Identifizierung der Oestragenwirkung des Hopfens Cosmetologie **22**, 21 (1959)
14) Corcilius F.: Stoffwechselbeeinflussung durch fluoreszierende Substanzen. Deutsch. Apoth. Ztg. **100**, 643-646(1960)
15) Leideritz H.: Hypericum perforatum—das Johanniskraut in der Kosmetik Parfumerie u. Kosmetik 7/1959
*) Neumann H.: Phytohormone, ein neuer Wirkstoffkomplex fur die Kosmetik. Parf. und Kosmetik **39**, 413-414(1958).
**) Product of Reimdiat GmbH, Augsburg, Germany

Emulsifiers

For ease of use — For dependable results —
For solving difficult problems

Tegacid...

Glyceryl Monostearate — Acid Emulsifying. For anti-perspirant — deodorant creams, lotions and ointments — all greaseless, medicated formulations.

Tegin...

Glyceryl Monostearate — Self Emulsifying. For neutral greaseless creams, lotions, ointments, suntan creams.

Tegin 515...

Glyceryl Monostearate — Non Self-Emulsifying. Used in conjunction with auxiliary emulsifiers.

Tegin P...

Propylene Glycol Monostearate — Self Emulsifying. For greaseless creams—brushless shave, foundation, suntan: lotions — foundation, suntan, ointments.

Lanolin Absorption Bases

PROTEGIN X.....ISO-LAN

For Creams, Lotions, and Ointments

• TEGOSEPT PRESERVATIVES ESTERS OF PARAHYDROXYBENZOIC ACID

• ANTIOXIDANTS PROPYL GALLATE ETHYL GALLATE

Goldschmidt
CHEMICAL CORPORATION

153 Waverly Place, New York 14, N. Y.

SALES REPRESENTATIVES

CHICAGO • LOS ANGELES • ST. LOUIS • MONTREAL • TORONTO

o-Phenylphenol,

a preservative worthy of reconsideration

By Eugene E. Wiese and Robert E. Moebius
The Dow Chemical Company

In recent years, considerable publicity has been given certain preservatives such as the p-hydroxy benzoates, sorbic acid, and dehydroacetic acid for cosmetic applications. So much so, that there is some indication o-phenylphenol and its sodium salts have been overlooked by cosmetic chemists.

Commercial o-phenylphenol(1) has been used extensively for many years in a wide range of industrial applications for control of bacterial and fungal degradation. Also, commercial o-phenylphenol has been successfully formulated into disinfectants for household, industrial, veterinary and hospital applications.

Experience with o-phenylphenol in these industrial applications has clearly demonstrated that it is a highly effective agent for microbiological control. Moreover, due to its low order of toxicity it has presented no problem of health hazard or handling.

Nevertheless, the application of the commercial grade of o-phenylphenol by necessity has been limited to those applications in which odor, taste, and color stability were not of major importance.

More recently purified grades of o-phenylphenol have been developed which overcome these limitations. Purified o-phenylphenol does not darken upon exposure to light but retains its light color for long periods of time. It has only a slight bland odor and taste that are characteristic of this compound.

o-Phenylphenol in this purified form can now be considered for these problems of microbiological control where low odor, taste, and good color stability *are of major* consideration.

Actually, purified o-phenylphenol has been and is being used by certain satisfied formulators in the pharmaceutical and cosmetic industry successfully.

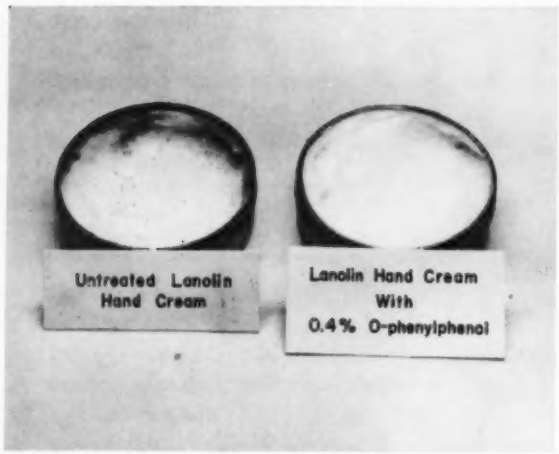
o-Phenylphenol has passed the all important test of practicability, since it can be employed effectively in the various emulsions, creams, moisturizing preparations and aerosols used today.

The appeal of o-phenylphenol lies primarily in its extremely low order of acute and chronic oral toxicity (2)—a rather dramatic property in view of its broad spectrum of activity against both gram positive and gram negative bacteria, as well as fungi.

In fact, the Food and Drug Administration has granted post-harvest residue tolerances for o-phenylphenol in or on a variety of raw fruits and vegetables(3).

Skin irritation and sensitization studies on o-phenylphenol have been carried out on 200 human subjects (100 of each sex) by the the Industrial Toxicology Laboratories of Philadelphia. When tested as a 5% solution in sesame oil it did not cause irritation or sensitization.

In tests conducted by the Industrial Toxicology Laboratories of Philadelphia vanishing cream base containing 0.5% Dowicide 1 was applied liberally to the right side of the face of fifty human subjects twice daily, in the morning and at night before



retiring, for 30 days. The vanishing cream base was applied in a similar manner to the left side of the face. The subjects were asked to spend at least eight hours a day in the sun every sunny day during the exposure period.

Daily examinations were made. Two weeks after the completion of the 30 day application, the challenge application was made. In these tests, it was found that none of the subjects showed any definite reactions due to the Dowicide 1 in the vanishing cream base during the course of the study. Four subjects reported some subjective complaints; in two of the subjects these complaints were produced by both the materials, in two others only the Dowicide 1 containing cream was involved.

As a result of these tests it was concluded that 0.5% Dowicide 1 in vanishing cream base did not exert primary irritating fatiguing, allergenic, or photosensitizing action. From a toxicological viewpoint, therefore, the use of Dowicide 1 at levels of 0.5% or less as a preservative or additive in vanishing type creams should present no problems, from ordinary repeated or prolonged skin contact in humans.

o-Phenylphenol has been evaluated as an antimicrobial agent against a large number of microorganisms. Laboratory tests show that o-phenylphenol is effective in killing gram negative bacteria in dilution of about 1:2000. Most gram positive bacteria are killed in a dilution in the range of 1:1700. Quantitative evaluation of o-phenylphenol against 12 different fungi showed that it killed in the range of concentrations of 0.015 to 0.005%. While in practical applications somewhat higher concentrations may be required, these tests reveal that o-phenylphenol has a wide spectra of activity against micro-organisms.

For evaluation of o-phenylphenol purified for microbiological control, it is suggested that a range of concentrations of 0.05 to 0.25% by weight of the formulation be considered.

References

(1) Orthophenylphenol is sold under the trade name Dowicide 1; sodium orthophenylphenate tetrahydrate is sold under the trade name Dowicide A by The Dow Chemical Company

(2) Hodge, H. C., Maynard, E. A., Blanchet, H. J., Jr., Spencer, H. C., and Rowe, V. K. Toxicological Studies of Orthophenylphenol (Dowicide 1) J. Pharmacol. Exptl. **Therap. 104(2)**: 202-210, 1952

(3) **Federal Register**, August 28, 1958

Allergies to cosmetic products

By Edward J. Masters, Ph.D., New York City

Helena Rubinstein, Inc.

Hypersensitivity is the principal factor in cosmetic dermatitis. While any manifestation of cosmetic allergy is of concern, the situation is not critical, and cosmetics as a class remains one of the least harmful of the commodities sold today.

It is estimated that approximately 10 per cent of the population is allergic in some form or other. The incidence of cosmetic allergy within this group is most difficult to estimate accurately. Sulzberger (1) patch-tested 998 patients exhibiting some form of dermatologic disease. Reactions to cosmetics were obtained in 3.8 per cent of those tested. Face creams, rouge, lipsticks, face powders, and eye cosmetics produced the reactions in diminishing order. A report on normal skin is not available.

Hjorth (2) reported that in 25,000 cases of patients with eczematous reactions examined over the course of the last twenty years, only 550 cases (2 per cent) could be ascribed to a cosmetic product as verified by a positive eczematous patch test. Creams, lipsticks, face powders, hair dyes, and nail lacquer in diminishing order accounted for the reactions.

The incidence of cosmetic allergy in people with normal skin can be expected to be substantially below the figures given of from 2 to 3.8 per cent.

An interesting summary covering a major cosmetic company's experience on complaints of reactions to its product is given later. This company's line of cosmetics is very broad covering over 150 products. For convenience the products have been condensed into categories listed in Table I. The number of reactions given include all complaints of alleged adverse reaction to the use of a specific product. The period of time covers a period of a number of years.

While undoubtedly all reactions were not reported, it is reasonable to assume that the summary includes all of the serious reactions. A total of 448 reactions in 113,601,535 units sold is good testimony to the general safety of cosmetic products.

Reprinted from the New York Journal of Medicine, for June 15, 1960

Depilatories when used in accordance with directions are efficacious and safe. Most depilatories on the market today use calcium thioglycolate in a cream or a lotion base. The pH of such depilatories is approximately 12. Although such depilatories can cause allergic reactions, the main cause of reactions where they occur is probably that of primary irritation.

Pertinent to this subject is the experience of Vestal (3) who reported his experience with the use of a commercial depilatory for presurgical preparation of patients. Over a period of fifteen months 460 patients were prepared for operation by the use of a detergent (pHisoderm or pHisoHex) and subsequent use of a depilatory. This treatment eliminated the use of razors, soap, alcohol, and the usual mercurial agent or other tinctures. No case of adverse reaction occurred.

Of special interest is the situation with hair dyes.

Table I.—Reactions Compared with Unit Sales

Categories	Reactions	Units Sold	Reactions per 100,000
Depilatories	120	3,146,937	3.9
Special cleansers	53	2,473,927	2.2
Permanent wave lotions	10	722,413	1.4
Hormone creams and lotions	32	3,458,880	0.9
Medicated creams and lotions	21	3,512,394	0.6
Suntan lotions and oils	3	553,459	0.6
Lotions	59	10,980,163	0.5
Eye products	57	11,581,279	0.5
Creams	16	4,277,700	0.4
Deodorants	12	3,900,503	0.3
Hair rinses	13	4,691,128	0.3
Miscellaneous hair treatment products	9	3,427,872	0.3
Shampoos	20	11,563,325	0.2
Makeup	11	9,364,612	0.1
Face powders	6	8,130,966	0.07
Lipsticks	3	13,455,431	0.02
Colognes and perfumes	3	17,703,055	0.02
Nail polish	0	657,491	0.00
Total	448	113,601,535	0.4

When hair dyes based on paraphenylenediamine were first introduced the incidence of reactions was quite high. There is no question of the severity of a paraphenylenediamine reaction when it does occur. Within the last five years, however, even with the more extensive use of such dyes, the incidence of reactions has become quite low. Improvement in the quality of the raw materials including the peroxide, better quality control, and an education of the consumer in regard to the proper use of such dyes may account for this better record.

Deodorants and Antiperspirants

Deodorants and antiperspirants represent a very important part of cosmetic sales amounting to approximately 50 million dollars at the manufacturer's level annually. Product distinction between deodorants and antiperspirants is disappearing. By appropriate formulation most products today combine the features of both and make claims for both effects. The deodorant effect of such products depends on the presence of antiseptics such as hexachlorophene or aluminum salts to inhibit bacterial growth. Sterile perspiration is generally odor-free, and the breakdown of the perspiration components through bacterial action or extraneous enzymatic action results in the formation of odor.

The metal salts of aluminum, zinc, and zirconium have been used for the purpose of inhibiting perspiration flow. The aluminum salts are particularly useful in having a dual action. Their effective bactericidal action has been demonstrated by Blank (4). In addition to their deodorant properties, the aluminum salts are effective antiperspirants.

The pH values of 20 per cent solutions of these salts are:

Salt	pH
Aluminum chloride	2.1
Aluminum sulfate	2.8
Aluminum chlorhydroxide	4.2

Aluminum chloride and aluminum sulfate both suffer the disadvantage of irritating primarily because hydrolysis results in an acid condition. In addition, unless properly buffered, they will damage clothing when the clothes are cleaned and subjected to the high temperature of a pressing iron. Aluminum chlorhydroxide in a 20 per cent solution is not a primary irritant and does little damage to fabrics; it is used in most of the antiperspirants sold on the market today.

The theory of antiperspirant action is interesting because of the disagreement as to what occurs. The traditional theory states that the aluminum ion combines with the protein of the skin forming metal albuminates and resulting in an astringent action with perspiration inhibition. In an official action, aluminum sulfate was described as an astringent which caused a swelling that contracted the openings of the sweat glands. Sulzberger (5) working with aluminum sulfate stated that he could find no support for the assumption of astringent action of antiperspirants with consequent narrowing of the sweat ducts. Pillsbury, Shelley, and Kligman (6) indicated that solutions of aluminum salts act as mild epidermal irritants that cause increased keratinization, resulting in a clogging of the sweat duct orifice and a consequent lowering of sweat flow.

Whatever the theory, antiperspirant action can be demonstrated and measured either by a gravimetric method (7,8), or by a color development method (9).

A properly formulated antiperspirant using aluminum chlorhydroxide is not an irritant and has little allergenic propensity. Within the last four years a number of deodorant products containing zirconium compounds have appeared on the market. Within this time, more than 60 cases have been reported involving the formation of granulomas in the axillae. In most of these cases, the use of a stick deodorant containing sodium zirconium lactate was involved. It was difficult to understand how compounds of zirconium which had been used extensively in poison ivy treatment could cause such reactions. Shelley and Hurley (10) investigated the problem and succeeded in reproducing the granulomas under controlled conditions. They were able to demonstrate the allergic nature of these reactions involving sodium zirconium lactate by injecting it intradermally into the sensitized subjects and obtaining a strong reaction. The allergic nature of the reaction was confirmed further by Shelley and Hurley (11) by injecting a 1 per cent solution of the salt intradermally and obtaining no reaction in a subject for six months. Subsequently a granuloma developed at the site of each injection, and the subject reacted quickly to new injections of the salt at low concentrations. Prior, Rustad, and Cronk (12) confirmed the toxic and sensitizing nature of sodium zirconium lactate. Both soap and hexachlorophene intensified the reaction of the skin to the zirconium salt.

Of interest is the experience of one manufacturer in marketing an antiperspirant formulation containing a combination of zirconium oxychloride and aluminum chlorohydroxide. (9) A sale of 500,000 units on a test-marketing basis generated a total of 4 complaints, none of which involved granulomas.

Prior and Cronk (13) reported on the effects of injections of zirconium tetraisopropoxide into albino rabbits. Significant reactions (nonspecific) were produced only when the zirconium compound was combined with hexachlorophene. Percutaneous application of the mixture produced no changes.

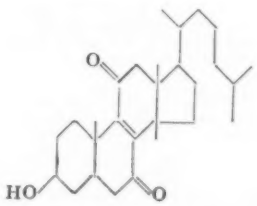
Lanolin

Anhydrous lanolin or wool wax, along with the many chemical modifications available today, represents one of the basic raw materials used in both the cosmetic and the pharmaceutical industries. In cosmetics its unique emollient and emulsification properties make lanolin an important constituent of lubricating creams, hand lotions, lipsticks, and related products. In addition, its good penetrant qualities make it most useful as an ointment base for active medicinal ingredients.

Lanolin and its derivatives are not primary irritants and allergic manifestations to its use are small. However, eczematous hypersensitivity has been reported (14–18). Sulzberger (19) in a controlled series of patch tests using lanolin and the constituents thereof found that 12 of 1,048 (1.14 per cent) subjects with an established history of allergic skin diseases reacted

positively to patch tests with pure lanolin. No positive reactions were obtained with lanolin in 120 healthy subjects. Inunction of lanolin on the uncovered skin produced a positive reaction in only 2 of 18 lanolin-hypersensitive individuals. Only 3 of these 18 subjects reacted to 5 per cent concentrations of lanolin and no positive reactions were obtained with 1 per cent concentrations. The aliphatic alcohols of lanolin were found to be responsible largely for the observed hypersensitivity of lanolin. Acetylation or propionlyation of such alcohols reduced or abolished their allergenic capacity.

Everall and Truter (20) demonstrated that the allergenic constituent of lanolin was an alcohol of structure:



They isolated another weakly allergenic compound: 7,11-dioxo-lanost-8-en-3-ol.

The detoxifying action (21) of lanolin is of considerable interest. The addition of adjuvants to diphtheria antitoxin such as tapioca powder increases the yield of antitoxin in horse serum. Guinea pigs injected with diphtheria toxin mixed with lanolin were able to survive forty lethal doses. Lanolin in this respect was far superior to such other adjuvants as calcium chloride, alum, and olive oil.

Another interesting physiologic action is the retardation of a benzypyrene-induced cancer growth by applying lanolin subsequently (22). Further indication of the lack of carcinogenic activity (23) is shown by the effects of intraperitoneal and subcutaneous injection of lanolin into rats. Such injection did not induce sarcoma, whereas the injection of liquid paraffin and yellow petrolatum did.

Various derivatives of lanolin are used widely in cosmetic manufacture. Such derivatives exhibit better physical properties and unique solubility characteristics. Depending on the product and specific problem, they serve as a superior replacement for lanolin. Generally such derivatives have lesser allergenic properties. A specific example of one of these variations is Lantrol, the liquid fraction of lanolin in which the heavy wax fraction has been removed by a solvent crystallization process. It is superior to lanolin as a skin penetrant and is emollient without the heavy unctuous feeling. This product does not exhibit allergenic properties when tested on subjects sensitive to lanolin.

Other derivatives of value are:

Trade Name	Description
Lanethyl	Alcohol soluble fraction of lanolin
Solan, Lanogel, G-1790	Polyoxyethylene derivative
Lanocerina	Fully hydrogenated lanolin
G-1425, G-1441, G-1471	Polyoxyethylene sorbitol derivative
Isopropylan, Isopropyl lanolate	Isopropyl ester
Modulan	Acetylated ester
Solulan	Ethylene oxide ether
Ricilan	Hydroxyesters made from castor oil and lanolin
Polylan	Polyunsaturated liquid ester of linoleic acid and lanolin alcohols

Orris Root

The allergenic character of orris root is well recognized and documented (24–28). The orris root of greatest commercial value is the rhizome of Iris pallida. On aging, the root develops a pleasant, woody violet scent. The powdered root has been used in face powders, in sachets, and in dry shampoos. Formerly, an interesting use of the root as such was to aid children in cutting their teeth (rhizoma iridis pro infantibus).

Steam distillation of the root produces the essential oil, orris concrete, in a 0.1 to 0.2 per cent yield. Further processing of the orris concrete results in absolute orris oil. Both oils are of value in perfume manufacture. Reported allergic manifestations are related directly to orris root as such and not to the oil.

There is apparently some misconception in regard to the present-day role of orris root as a raw material in cosmetics. Very little, if any, orris root is used in the cosmetic industry today. Most of the orris root sold today is to manufacturers for use in the adhesives for Band-Aids and back plasters.

Perfume Oils

Dermal reactions from perfume oils generally result from allergic hypersensitivity rather than from primary irritation. There is little definitive work in this field. Klarmann (29) has reviewed this subject exhaustively. The subject is highly complicated by the problems of chemical composition and by wide quality variance even in the same class of perfume oil.

There are approximately 5,000 odoriferous substances in general use today. The approximate concentration of perfume oils used in cosmetics generally is 0.5 per cent, in colognes 4 per cent, and in perfumes up to 20 per cent. Such perfume oils contain 50 or more basic components. In the case of a sensitivity reaction, the pinpointing of a specific perfume oil component as the sensitizer is a formidable task.

Photosensitization is an effect associated with a number of essential oils: neroli, petitgrain, cedarwood, lavender, and bergamot. Berlocque dermatitis has been shown to be caused by oil of bergamot. The dermatitis is manifested by a pigmentation of the skin after exposure to sunlight following application of the perfume oil. The photosensitizing agent in oil of bergamot is not known. Chlorophyll, traces of copper, and psoralens, in turn, have been named as the responsible agents. It is interesting to note that the sensitization occurs with freshly pressed bergamot oil. Purification or aging of the oil eliminates or reduces its sensitizing propensity.

The chemical kinship of the essential oils is such to make the range of oils to which a sensitive person will react quite broad. Keil (30) showed that a num-

ber of patients sensitive to oil of citronella were also sensitive to oil of lemon and mutual components of both. Another patient reacted positively to oil of lemon and oil of turpentine. This patient reacted also to alpha- and beta-pinene (chemically related to limonene). An allergenic effect of interest is that of inhalation sensitivity to various citrus oils shown by some. (31)

A recent development of considerable interest is the creation of a series of perfume oils of low-sensitizing potential called Chemoderms (32). A group of 82 raw materials which were chemically reproducible, especially purified, and screened by patch test to eliminate proved skin sensitizers were used to formulate a series of 10 perfume oils. The low-sensitivity capacity of these oils was established by both patch and use tests.

Hypoallergenic Cosmetics

The term "hypoallergenic" when applied to cosmetics has no definite legal or official status. It was coined as a permissible substitute for the word "nonallergic." "Hypoallergenic" is applied to those cosmetics formulated especially for use by individuals who are sensitive to certain ingredients of cosmetics. There is no standard which measures the hypoallergenic quality of a product. Rather the term describes a specific kind of technical and marketing approach. From a technical standpoint, when a hypoallergenic cosmetic is formulated, raw materials are screened carefully and those with even limited sensitizing capacity are not used. In principle, the resulting cosmetic is less likely to cause an allergic reaction in the user.

A number of companies cater to the specific problems of the allergic woman and aid her in solving her particular cosmetic problem through her allergist or her dermatologist. Where this is so, the term hypoallergenic is meaningful, and a function of value is performed. However, where such products are sold generally to the public, no significant difference exists between such products and those marketed by reputable manufacturers. In actuality, the allergenicity in cosmetics thus distributed has been reduced to the minimum.

References

1. Rostenberg, A., Jr., and Sulzberger, M. B.: Some results of patch tests, A.M.A. Arch. Dermat. & Syph. **35:** 433 (Mar.) 1937.
2. Hjorth, N.: Cosmetic allergy, J. Soc. Cosm. Chem. **10:** 96 (1959).
3. Vestal, P. W.: Preoperative preparation of the skin with a depilatory cream and a detergent, Am. J. Surg. **3:** 398 (Mar.) 1952.
4. Blank, I. H., Moreland, M., and Dawes, R. K.: The antibacterial activity of aluminum salts, Proc. Scient. Sec. Toilet Goods A. **27:** 24 (May) 1957.
5. Sulzberger, M. B., Zak, F. G., and Herrmann, F. J.: Studies of sweating; on the mechanism of action of local antiperspirants, A.M.A. Arch. Dermat. & Syph. **60:** 404 (Sept.) 1949.
6. Pillsbury, D. M., Shelley, W. B., and Kligman, A. M.: Dermatology, Philadelphia, W. B. Saunders Co., 1956, chap. 36, p. 832.
7. Fredell, W. G., and Read, R. R.: Drug & Cosm. Indus. **69:** 49 (1951).
8. **Ibid.:** **74:** 468 (1956).
9. Daley, E. W.: Antiperspirant testing, Proc. Scient. Sec. Toilet Goods A. **30:** 1 (Dec.) 1958.
10. Shelley, W. B., and Hurley, H. J.: Allergic origin and zirconium deodorant granulomas, Brit. J. Dermat. **70:** 75 (Mar.) 1958.
11. **Idem:** Experimental evidence for an allergic basis for granuloma formation in man, Nature, London **180:** 1060 (Nov. 16) 1957.
12. Prior, T. J., Rustad, H., and Cronk, G. A.: Benzophenones; ultraviolet light absorbing agents, J. Invest. Dermat. **29:** 449 (Dec.) 1957.
13. Prior, J. T., and Cronk, G. A.: Pathological changes associated with aluminum and zirconium compounds, A.M.A. Arch. Dermat. & Syph. **80:** 447 (Oct.) 1959.
14. Sulzberger, M. B., and Morse, J. L.: Hypersensitiveness to wool fat, J.A.M.A. **96:** 2099 (June 20) 1931.
15. Milian, G., and Garnier, G.: Dermatose des tondeurs de moutons, Bull. Soc. franc. dermat. et syph. **43:** 1473 (July) 1936.
16. Sezary, A.: Intolerance cutanee a la lanoline, Presse med. **44:** 1880 (Nov. 18) 1936.
17. Fanburg, S. J.: Dermatitis due to aquaphor, A.M.A. Arch. Dermat. & Syph. **42:** 479 (Sept.) 1940.
18. Ellis, F. A.: Allergic contact dermatitis due to wool fat and cholesterol, **ibid. 56:** 801 (Dec.) 1947.
19. Sulzberger, M. B., Warshaw, T., and Herrmann, F.: Studies of skin-hypersensitivity to lanolin, J. Invest. Dermat. **20:** 33 (Jan.) 1953.
20. Everall, J., and Truter, E. V.: Cutaneous hypersensitivity to lanolin; investigation of one case, **ibid. 22:** 493 (June) 1954.
21. Lemetayer, E., Ramon, G., and Richou, R.: Sur l'injection a l'animal d'experience de la toxine diphterique en melange avec differentes substances, en particulier avec la lanoline, Compt. rend. soc. biol. **118:** 108 (1935).
22. Hatschek, R., and Rogicky, J.: Chem. Zent. **2:** 1718 (1943).
23. Reiter, A., and Schmachl, D.: Arzneimittel-Forsch. **3:** 403 (1953).
24. Balyeat, R. M.: The importance of orris root as an etiologic factor in hay fever and asthma, J. Lab. & Clin. Med. **3:** 516 (Feb.) 1928.
25. Feinberg, S. M.: Seasonal hay fever not due to pollen, Ann. Int. Med. **3:** 1035 (Apr.) 1930.
26. Malone, J. T.: Allergy to orris root (rhizome) powder as an etiological factor in Meniere's disease; report of 2 cases, M. Bull. Vet. Admin. **9:** 406 (Apr.) 1933.
27. Frickman, L. E.: Common allergens: orris root, Proc. Staff Meet. Mayo Clin. **9:** 291 (May 16) 1934.
28. Muldoon, W. E., and Kahn, I. S.: Local allergy of the eye due to orris root, Texas J. Med. **33:** 822 (Apr.) 1938.
29. Klarmann, E. G.: Perfume dermatitis, Ann. Allergy **16:** 425 (July-Aug.) 1958.
30. Keil, H.: Contact dermatitis due to oil of citronella, J. Invest. Dermat. **8:** 327 (June) 1947.
31. Urbach, E.: Odors (osmyls) as allergenic agents, J. Allergy **13:** 387 (May) 1942.
32. Osbourn, R. A., Tusing, T. W., Coombs, F. P., and Morrish, E. P.: Dermatologic standardization of perfumes, I, New York State J. Med. **57:** 1069 (Mar. 15) 1957; II, **57:** 1391 (Apr. 15) 1957.

WONDERFUL WORLD OF FRAGRANCE

With creative research and modern production facilities in every major marketing area of the free world, IFF develops and produces the persuasive fragrances that give sales appeal to successful consumer products the world over.

The right fragrance for your new product...an exclusive IFF creation.

Still Room at the IFF plant, Union Beach, N. J., where the most advanced high column vacuum distillation equipment produces, in quantity, the purest aromatic materials for making fine fragrances.

iff

van Ameringen-Haebler *division*

INTERNATIONAL FLAVORS & FRAGRANCES INC.

521 West 57th St. • New York 19, N.Y.

Leading Creators and Manufacturers in the World of Fragrance

ARGENTINA · AUSTRIA · BELGIUM · BRAZIL · CANADA · ENGLAND · FRANCE · GERMANY · HOLLAND · INDONESIA · ITALY · NORWAY · SOUTH AFRICA · SWEDEN · SWITZERLAND

for any anti-perspirant base

IT'S WISE TO
COME TO REHEIS FIRST

No other supplier produces as many grades of the basic ingredient for anti-perspirants as Reheis.

Choose from *five* different forms of Chlorhydrol® . . . granular, fine, medium, impalpable, and 50% w/w solution . . . for the perfect type for your cream, lotion, spray and powder formulae.

For your stick deodorants, there's Chloracel® . . . a 40% w/w solution or powder for alcoholic sticks.

And *all* Reheis anti-perspirants are *safe* . . . won't destroy fabrics or irritate skin. Do not require buffering.

Available in any quantity from stock.

That's why it's wise to come to Reheis first for anti-perspirant supplies or technical help. For detailed information, write to:

REHEIS FINE CHEMICALS®

REHEIS COMPANY, INC.
Berkeley Heights • New Jersey
manufacturers of
Fine Chemicals

Mixing of pharmaceutical solids: the general approach

By David Train

It is important to have a suitable criterion for good mixing for pharmaceutical solids, because the attainment of an accurate dosage of a small quantity of a potent drug so often depends on the thoroughness by which it is dispersed through the bulk of another, or other materials. Mixing the solids, of necessity, presupposes the particulate form, and there are certain factors and properties associated with particles that will always affect the results of a mixing operation. It is the purpose of this paper to review these factors and properties, and also the operation, so that desirable criteria and possible practical procedures may be assessed rationally when a specific problem in solid mixing is being considered.

Consider an assemblage of particles or a static powder bed before any mixing process begins. All particles are subject to a constant force of gravity and they are in some sort of spatial equilibrium with one another. As long ago as 1885 Osborne Reynolds (1) showed that in order to obtain relative particulate movement within such a bed, the volume of the bed must be increased. Subsequent work by Jenkin (2), and by Brown and Hawksley (3) have amply confirmed that even in the case of a randomly packed bed, no appreciable movement can take place while the bed is in the condition that it spontaneously takes up as it is formed. Brown and Hawksley found that movement in a bed was produced by failure along a slip line or, in other words, a shear movement. For such a movement to take place, there must be sufficient space between the particles and this provides the first necessary condition for mixing. Assuming there is a preliminary condition of partial or total segregation, it follows that mixing must be achieved by some form of interparticulate movement, and this can only take place if the bed of particles is expanded. The extent to which a powder mass may be made to dilate is a complex function of the physical properties forming the system, but a good empirical test is to compare the specific volume of a tapped bed (4) with the specific volume of the same bed which is on the point of being fluidized. The ease with which movement could take place is, within reason, a direct function of the degree of expansion which can be produced in the specific volume of the particulate system. Practically, this means that there should be sufficient room in a mixing container to allow the powder mass to dilate, and it also points to the risk of loss of economic efficiency if the space in a given mixer is overfilled.

Assuming interparticulate movement is possible, then, in order to produce such movement, suitable forces must be applied to the particles. Since continued application of pure tensile or compressive forces will serve only to increase or decrease the specific volume of the system without the particles

[Reprinted from the **Journal of the American Pharmaceutical Association**, Scientific Edition, Vol. 49, No. 5. May 1960.]

changing stations relative to one another, it follows that shear forces will be necessary to produce interparticulate movement. See Fig. 1. Because the force of gravity is constantly applied, a vertical force either reduces or reinforces the vertical stress according to whether its direction is upwards or downwards. Any horizontal component of force acts at right angles to the gravitational force, and will, in combination with the vertical force, automatically induce a shear stress into that part of the system. If the system is incapable of resisting such a stress, movement along a slip plane takes place.

The forces are introduced by some external means and, by interparticulate transmission, act within the bed. To ensure mixing there must be such movement that each and every particle could visit, if given time, every point within the confines of the system in its expanded state. This requires a three-dimensional stress system which will induce movements in all planes. To ensure rapid, and therefore economic, mixing it is necessary to cause the greatest possible number of slips per unit of time. If adjacent slip planes are produced so that they are not more than one particle apart then there will be movement between all particles.

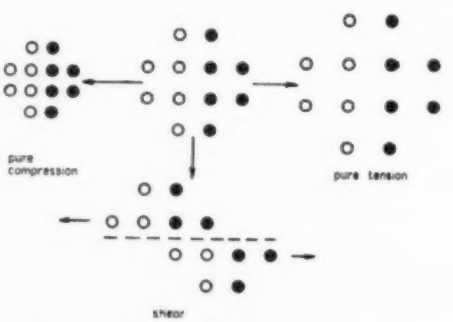


Fig. 1.—Action of forces acting on a particulate system.

These considerations give, *a priori*, requirements of any apparatus to be used for mixing solid particles. The specific volume of the system must be suitably increased to give freedom of movement to the particles. Forces must act so that a three-dimensional grid would be necessary to plot the lines of movement of each and every particle. These forces must be such that, in time, each particle could visit every point within the confines of the particulate system in its expanded condition. Finally, when all movement ceases the system must be able to take up a state of static equilibrium without segregation of particles taking place. Applied to any specific situation three possible causes of inefficient mixing are highlighted: *(a)* Insufficient dilation of the bed, either generally or locally; this causes hindrance to particle movement and in its mildest form causes increased time for mixing, and under the worst conditions would prevent any possibility of proper mixing being achieved. *(b)* Induced forces being insufficient to produce suitable movement in all directions, thus leaving portions of the assemblage undisturbed. This can be manifest as movement in two axes only as in a simple cylindrical drum revolving horizontally about its axis when there is little or no lateral particulate movement. Inadequate forces may allow the presence of dead zones within a system, or may allow aggregates (loose assemblages of particles held together by light cohesive surface forces such as those caused by water films or electrostatic charges) to move round as compound entities, within which no relative movement or particle exchange takes place. *(c)* Preferential movement of a certain type of particle due to dissimilarity of physical property (e. g., size or density) of materials being mixed. This can be the cause of imperfect mixing, however long the operation is allowed to proceed, or segregation as soon as mixing conditions change, such as stopping at the end of the process.

Effects produced by dissimilar particles and surface-active forces

Before considering the criteria for mixing, it is necessary to summarize the effects produced by certain physical conditions which can occur in the materials to be mixed.

First, there is the difference in size between particles. Coulson and Maitra (5) have reported careful investigations using a simple drum mixer with its axis set at an inclination of 23° to the horizontal because this angle gave best mixing conditions. They found that if fine particles were put at the bottom of the drum and coarse particles of the material placed on top, no mixing occurred. When the position of the sizes was reversed, the larger being on the bottom, then mixing did occur for a short time but segregation developed as the coarse particles rose to the top of the bed. The reason for this difficulty of producing or maintaining a mix with particles of different sizes is due to the small particles being able to fall through the void spaces between the large ones. See Fig. 2. A small particle, $d = 0.41D$, can just slip between four larger particles touching in a square grid, while a particle $d = 0.15D$ can just slip between three larger particles touching on a triangular grid.

Practically, it must be recognized that with any mixing apparatus, there is always a tendency for segregation if there are large differences in particle sizes. It is also important to note that even if a true mixture is obtained, the condition is unstable and will separate rapidly if subjected to vibration in storage or subsequent processing. Thus, although it must be accepted that some mixtures have to be made with materials of different sizes, it should always be the aim to mix components with the same size range and the closer the range, the simpler the operation.

A second condition may be caused by a density difference between the component materials. The effect is not so marked as that of difference in size, but Coulson and Maitra showed that the rate of mixing was impeded by an increase in density difference. This was supported by Gray (7) who also found that there was a tendency for segregation to develop with time of mixing in the case of certain systems, like the concrete mixer. The prevention of segregation in this case requires a condition of vigorous movement between the particles coupled with a restriction on freedom to move in order to prevent segregation under free falling conditions. This is a

difficult specification to comply with in practice. Machines which reverse the gravitational field help to reduce the adverse effect of density difference. Again vibration during subsequent processing or storage will help to produce segregation of the mixture.

The effect of particle shape on mixing conditions has not been extensively investigated, but it is well known that roughly equidimensional particles are easier to mix than any other shape. The addition of flat or acicular particles prolongs the mixing time because of their tendency to bundle, and vigorous treatment is often required to break up such assemblages.

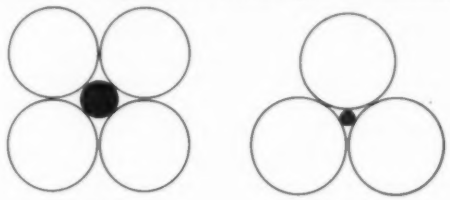


Fig. 2.—Small particles slipping between large particles.

The fourth condition is the part played by surface-active forces so that groups of particles are held together as aggregates and consequently do not disperse evenly through the other components. The forces which produce this are mainly surface tension due to adsorbed liquid films, electrostatic charges, or possibly to weak Van de Waals forces. Since the forces act on the surface of the particle, their effect becomes greater as the specific surface area of the solid increases, that is, as the absolute particle size becomes smaller, and produces powders which have high angles of repose and poor flowing characteristics. Andreasen (8) made some investigations into the "stickability" of powders and found that, in those materials which had a propensity to aggregate, the effect became very marked with particles smaller than 10 μ. This figure is quite arbitrary but it is a useful one to use because it conveniently provides an upper size limit of what could be subjectively called a "very fine powder." Neumann (4) was interested in setting up an index of "stickiness" and she achieved this by a technique developed by Hawksley (9). Briefly, she found out how much of a coarse granular material she required to add to a given sticky powder in order to make the resultant mixture have certain flow characteristics so that it would maintain a steady flow through a standard orifice. The results for a selection of powders is given in Table I.

To explain the change in conditions produced in the powder, Andreasen postulated that the fine particles were adsorbed onto the surface of the large particles and as the mass of a large particle was sufficient to overcome aggregation by surface forces, the material became free flowing. As an investigation, Andreasen's experiments were successful, but the inferences must be applied with care to the mixing of pharmaceutical powders. For example, there is no evidence that all the aggregates of fine powder are broken up when sufficient coarse material has been added to make the mixture flow. Thus, compound particles can still exist and dispersal on a microscale is patchy and irregular even though the random distribution of the large particles through the mix may be perfect. Also, Andreasen was concerned with making a powder with poor flow qualities free flowing; he did very little to investigate the extent of segregation which can be produced with such a mixture under suitable conditions of subsequent processing and storage.

With the foregoing as a basis it is now possible to select a few examples to illustrate some of the inherent limitations in performance of various types of mixing equipment. Reference has already been made to the poor mixing ability of a simple cylindrical drum revolving about its axis because most of the individual particulate movement within is in one plane only. Various mechanical devices have been introduced from time to time to overcome this weakness. The addition of helical flights in one form or another was probably the first modification, and of recent years, revolving the drum with its axis at an angle to the horizontal, or on an axis which is at an angle to an axis of symmetry and to the direction of gravity, has been used successfully on a commerical basis. Into this category, too, may be placed the rotating cube-type mixer. The Z-blade mixer and planet mixer exhibit other variations in that movement is induced by impellers, while the container remains stationary. All techniques induce a skew movement on the particles as they fall under the influence of gravity. This enhances the mixing quality of the system, and is usually successful for mixing free flowing particles of even density. If density differences have to be accommodated then mixers producing a periodic abrupt reversal of flow of the powder, such as the double, V-, or Y-cone mixers with baffles are the equipment of choice. However, in all types of plant mentioned above it must be remembered that intensity of shear between particles is mild, and while little or no attrition of other particles may be a desirable property in the case of blending free flowing powders, the break-up of closely held aggregates of small primary particles of a specific ingredient is an inefficient process.

Because size reduction equipment relies almost exclusively on the principle of shear to break down solid material, it is to be expected that most types of plant used for this process have, at one time or another, been utilized for mixing powdered solids. Shear forces in mixing are especially important to help the break-up of the compound aggregates into primary particles. The use of such plant, however, means reducing in size by mechanical breakage at least a proportion of the particles. That this will

Table I.—Stickiness of Powders

Material	Mean size, μ	Sand Required to Produce Free Flow, %
Catalyst microspheres	25	0
Calcium fluoride	30	0
Anhydrous sodium carbonate	100	23
Titanium dioxide	0.5	26
Refined kaolin	2	1,200
Natural fuller's earth	0.1	25
Activated fuller's earth	5	60
Cement	10	100
Flour	25	30

happen is often anticipated and in such cases ingredients, which are initially oversize, are fed in the correct proportions into the plant and are reduced and partly mixed in one operation. It must be emphasized that although size reduction machinery is used for the mixing process because of the shear forces used, this does not necessarily make such plant good mixing apparatus; there may be efficient incidental mixing on a local scale, but general mixing either does not take place or if it does, proceeds slowly and may therefore be uneconomic.

Muller-type reducers, as exemplified by the pestle and mortar, the end or edge runner mills, or the buhr-stone mill, produce a shearing action between two surfaces moving parallel to the plane of contact. Only a small portion of the material is being processed at any one time and general mixing is slow because the bed is virtually in an unexpanded state and there is little relative movement in the bulk of the particles except near the zone of the muller.

With size reducing plant using impact principles, such as the pin disk mill, the hammer mill, or the fluid energy mill, intense shear forces on a local scale produce a breakdown to primary particles and turbulent air currents ensure mixing of any particles which happen to be in the plant at the time. However, the hold-up capacity of such machines is usually low, so that little or no general mixing is possible and therefore this must be done by other means.

Sieving and sifting techniques have often been recommended as suitable for aiding a mixing process, on the basis that a sieve helps to break up an aggregate or a concentration of an ingredient into primary particles, or, alternatively, the meshes act as simple proportioning device and redistribute the material as it lands on the sieve. This second premise is probably correct and is a useful procedure when the size of the holes is large compared with the dimensions of the particles. The basis for breaking down aggregates is not so well founded however, because a mesh size must be selected which is only a little larger than the large particles. Since, on a probability basis, the smaller particles will tend to pass through first, it follows that there will always be a segregation on a particle size basis during the process, thus defeating the object of mixing.

Pharmaceutical requirements of the mixing operation

Having set out the principles of mixing and briefly reviewed the limitations of the apparatus used to achieve it, it is necessary to consider the use to which this operation is put. Pharmaceutical materials are being mixed and therefore, by implications, are essentially for medicinal or veterinary use. The physician or veterinarian prefers to use medicaments which produce precise and dependable effects. This can only be achieved by using carefully standardized materials in exact quantities, and the pharmaceutical world has built up a reputation for supplying most of its dosage forms in this manner by suitable process and analytical control. To be successful such control has to be used intelligently, and this applies especially in the case of any dosage forms involving the use of mixtures of powders. Much has been said and written about the procedure for sampling particulate matter when every effort is made to obtain a representative sample of a batch of material. Such routines are correct when a commercial transaction is involved, for it is an assessment of the average content of the ingredients that is required. But when a powder is to be used as the basis for a medicine, then it is the actual content of a specific single dose which must be the criterion for control and sets what has aptly been named "the scale of scrutiny" (6).

The concept may be clearer to understand if one quotes a few examples: the scale of scrutiny for a foot powder or a dusting powder is the amount of an average application; for an internal medicine it is the dose unit or minimum normal dose, a teaspoonful of effervescent granules, the contents of a capsule or cachet, a suppository, or a tablet.

The physician and patient have every right to expect that the stated amount of medicament is, in fact, present in each and every dose product and that the acceptable variations of amount fall within precise and, preferably stated, overall limits. Mixtures of powders and products derived therefrom may, in fact, fail to comply with this requirement. The final analytical control provides the last check to ensure that the product contains the stated dose of medicament, and it follows from medical requirements that the analytical techniques adopted should, and even must be able to, check adequately the magnitude of minimum unit dose and also provide assessment of the possible variations in amount per unit dose due to limitations in manufacturing procedures.

The ideal condition is to be found in a simple random analytical sample, the size of which is smaller than the minimum unit dose, in which the analyst is confident that his analysis truly represents the specification of the bulk of the material and would be identical with that of any other random sample of the same size. In this case it may be unreservedly assumed that any dose unit contains the required amount of medicament. Such a condition is found in medicaments in the form of simple solutions with low viscosities of say less than 10 centipoises. If, however, the size of the analytical sample exceeds the normal minimum dose, uncertainty of the accuracy of the dose must always exist to a lesser or greater extent according to the number of dose units which are used to make up the analytical sample. This is because there is the possibility of variation in content within the units comprising the sample. From a physician's or patient's point of view, these unknown variations will be in addition to those included in the range allowed by the analysis as well as those inherent in measuring the dose unit concerned. These unknown variations will be small or nonexistent in materials which can be adequately mixed but in the case of materials which are difficult such as powders, they can be quite large so that apparently identical unit doses could produce important differences in pharmacological response.

To illustrate this point reference should be made to the official requirements for some products of powders, i. e., tablets, in the U. S. P. XV and B. P. 1958. (See Table II.) The smallest dose in which the medicament is normally prescribed has been selected because

Table II.—Relation Between Minimum Unit Dose and Analytical Sample of Selected Tablets in U. S. P. XV and B. P. 1958

Ref.	Medicament	Analytical Limits, %	Scale of Scrutiny, Dose, mg.	Assay Sample: Dose Units Used	Assay Sample: Wt. as Active Principle, mg.	Analytical Sample: Wt. as Active Principle, mg.	Analytical Sample: Equivalent Dose Units
B. P.	Acetomenaphthone	92½—107½	0.5	400	200	200	400.0
B. P.	Ascorbic acid	90—110	25.0	20	500	50	2.0
U. S. P.	Atropine sulfate	90—110	0.3	200	60	60	200.0
B. P.	Carbimazole	90—110	5.0	20	100	6	1.2
U. S. P.	Colchicine	90—110	0.5	50	25	25	50.0
U. S. P.	Cortisone	90—110	25.0	10	250	25	1.0
B. P.	Cortisone	90—110	25.0	20	500	10	0.4
U. S. P.	Digitoxin	90—110	0.1	50	5	2	20.0
U. S. P.	Reserpine	90—110	0.1	20	2	1	10.0
U. S. P.	Stilbestrol	90—110	0.1	100	10	10	100.0

it is in this condition that, between doses, the greatest variation is possible. It will be seen that 400 acetomenaphthone B. P. dose units or 200 atropine sulfate U. S. P. dose units are required to produce a minimum analytical sample. Thus the variations to be found between 200 individual doses of atropine sulfate have been averaged to give a mean content of drug with an allowable error of 10% about the stated content. Thus any imperfection of mix in any one tablet will be masked by the contribution made by 199 units which also form the analytical sample. On the other hand only two-fifths of the minimum dose of cortisone is required as the analytical sample for the B. P. assay yet the analyst has been required to take 20 such dose units to make his sample. Other examples speak for themselves. It will be seen that the emphasis has been to obtain a reasonable mean and is probably favorable to the manufacturer. Products only fail to pass the test if there has been a gross error of judgment in manufacture when, correctly, the batch should be rejected.

It has been deemed necessary to check the uniformity of weight of individual products, but no method is given or suggested so that the uniformity of mix may be checked on a minimum dose unit scale. Thus the uniformity of mix of the ingredients is left to the inherent mixing capability of the machine and the integrity of the operator to run the machine to give the optimal conditions of mix if he knows them.

In practice, where the pharmacological intention of the dose is to correct a deficiency or maintain a medication, as in ascorbic acid or digitoxin, the patient's body probably can accommodate the possible product-to-product variation in dose, but when the analytical sample rises above 50 dose units, the course of treatment must be long before it can be safely assumed the patient has taken a mean dose consistent with the mean content as shown by analysis. When medication depends on the effect produced by only one or two dose units, then it is reasonable to assume that sufficient attention is paid to the checking of individual dose units. It should be a matter of professional pride that this is done. However there are certain principles of probability which come into the process of mixing and these must be clearly borne in mind when a mixing procedure or checking scheme is being developed.

Because there is a trend towards dry mixing of powders for slugging in tablet manufacture and for filling capsules, it is a useful exercise to assess the statistical aspects of obtaining a unit dose with the correct proportion of ingredients from a truly randomized bulk mixture of equal sized particles of ingredients present in their correct proportions. The probability of obtaining a sample containing the correct proportions of the ingredients varies with the number of particles taken for the sample (10). Thus, in taking samples from an infinite supply of a 50:50 mixture of P and Q, a sample of n particles will on an average contain $n/2$ particles of P. But any one sample may contain less than this number with a corresponding increase in Q. The error to be expected can be expressed mathematically in the form given by the standard deviation about the mean, and it can be shown that multiples of the standard deviation may be used to determine confidence limits to give the proportion of samples, consisting of a given number of particles, that would have less than a given variation in the proportion of a selected ingredient.

For example (See Table III), in the case of a 50:50 mixture, the standard deviation of one component, expressed as a percentage of the whole, is given by $100/\sqrt{n}$, where n is the number of particles in the sample. This means that if a sample of 100 particles were taken, one could be confident that 68.3 per cent of samples would have less than a 10 per cent error in the proportion of P, and in like manner 95.5 per cent of samples would have less than a 20 per cent error, while 99.7 per cent samples would

Table III.—Perfect Mixing[a]

Confidence Level of No. of Samples	% Limiting Error in p: n = 100	n = 10,000	n = 1,000,000
68.3	10	1	0.1
95.5	20	2	0.2
99.7	30	3	0.3

[a] Proportion of P:Q = 50:50; no. of particles in a sample n; standard deviation of sample, % = $100/\sqrt{n}$.

Table IV.—Perfect Mixing[a]

Confidence Level of No. of Samples, %	% Limiting Error in p: p 0.01 n 900	0.01 250,000	0.025 1,000,000
68.3	30	2	2
95.5	60	4	4
99.7	90	6	6

[a] Proportion of P:Q = p:1-p; no. in sample = n; standard deviation of sample, % = $100/\sqrt{pn}$.

have less than a 30 per cent error in P. If the sample size n, were raised to 10,000 particles the errors for each confidence level will have reduced to 1, 2, and 3 per cent, respectively, while if n is a million particles, the errors will have been reduced to 0.1, 0.2, and 0.3 per cent of the desired proportion.

If, however, the proportion of one ingredient is small (see Table IV), then the standard deviation from the mean of the proportion of a given ingredient, expressed as a percentage, may be estimated by $100/\sqrt{pn}$, where p is the proportion of the material expressed as a fraction and n is the number of particles in a sample. It will be seen that for a 1 per cent dispersion and a sample of 900 particles, the confidence levels will be as follows: 68.3 per cent samples would have less than 30 per cent error in the proportions of P, 95.5 per cent samples would have less than 60 per cent error in the proportions of P, and 99.7 per cent samples would have less than 90 per cent error in the proportions of P. To assume reasonable errors of 2, 4, and 6 per cent, respectively, the total number of particles per sample must be of the order of 250,000. Applied to dry mixing of powders, this means that for a dose of 1 mg. of drug in a product weighing 100 mg. the total material should be reduced in size to give at least 250,000 particles so that the unit dose, based on a perfect mixing operation alone, may be within 4 per cent of the correct dose for 95.5 per cent of the products and within 6 per cent for 99.7 per cent of the products. Assuming that the drug and diluent have a specific gravity of 1.5, the mean particle size of all ingredients must be less than 50 μ.

One of the smallest doses in either pharmacopeia is 0.1 mg. Assuming that this is to be presented as a 40-mg. dose unit, the dilution is 1 in 400. Working to the same confidence limits as the preceding example, the unit sample should contain at least 1 million particles so that the mean particle size should be less than 4 μ.

It must be emphasized that the foregoing calculations have been based on a condition of perfect mixing. If this is not obtained, the variation in behavior between unit doses is subject to additional errors. It is clear that the operation of powder processing is by no means understood or worked out and that the worst enemy in this field is probably complacency through ignorance. Pharmaceutically it must always be the aim to supply precise individual dose units, but it must be concluded that present day practices in powder technology sometimes fall short of this attainment.

References

(1) Reynolds, O., **Phil. Mag., 20,** 469(1885).
(2) Jenkin, C. F., **Proc. Roy. Soc., A, 131,** 53(1931).
(3) Brown, R. L., and Hawksley, P. G. W., **Fuel, 26,** 159(1947).
(4) Neumann, B. S., "Flow Properties of Disperse Systems," Interscience Publishers, Inc., New York, N. Y., 1953.
(5) Coulson, J. M., and Maitra, N. K., **J. Imp. Coll. Chem. Eng. Soc., 4,** 135(1948).
(6) Anon., **Brit. Chem. Eng., 1,** 29(1956).
(7) Gray, J. B., **Chem. Eng. Progr., 53,** 25(1957).
(8) Andreasen, A. H. M., Hofmanbank, N., and Rasmussen, N. H., **Kolloid-Z., 86,** 70(1939).
(9) Hawksley, P. G. W., **Pulverised Coal Conference, 1947,** 679.
(10) Saunders, L., and Fleming, R., "Mathematics and Statistics," Pharmaceutical Press, London, England, 1957.

Abstracts of papers given at the symposium on

The Scientist's Contribution to the Safe Use of Cosmetics

sponsored by

The Committee on Cosmetics, American Medical Association

in cooperation with

The American Association for the Advancement of Science

presented before the Pharmacy Section (NP) at the

127th Annual Meeting of the AAAS

New York City, December 29, 1960

Some Problems of Biological Research and Their Relation to Cosmetic Development and Use

William Montagna, Ph.D.
Department of Biology, Brown University

In spite of belief to the contrary, there are no profound differences between basic and applied research. Those of us who have an academic interest in the biology of skin realize that the biologist, the dermatologist, and the cosmetic chemist share the same problems, and that they are all searching for the same things. The essential difference between them is in their motivation for research and in the way that they plan to use their information.

The interest of the cosmetic chemist is in compounds that beautify and/or improve the health of the skin. The most important feature of these compounds is that they must not clash with the normal properties of skin. The cosmetic chemist, therefore, must have at his disposal a catalog of the total spectrum of the biological properties of skin. He must understand that the skin of the same individual is a heterogeneous organ system which is remarkably different in the various regions of the body. Also, numerous and dramatic changes occur in the skin of an individual during the period of growth and development and during the period of ageing and senility. Growth and differentiation cease neither at birth nor at the completion of the growth in stature but continue throughout life. Skin, then, is an organ that possesses many of the potentialities of embryonal tissue, with still unknown mechanisms that control growth and differentiation. Since the various end-products of the cutaneous appendages are very different, the chemical and physiological attributes of each of the cutaneous appendages are also different.

Since the major function of skin is that of protection against the invasion of foreign agents, it resists the penetration of many substances. We must know, therefore, what substances penetrate through it and what substances do not. If some materials do penetrate, one must know their portal of entry and the biological reactions that these substances have with the skin. This is pertinent to the topical application of vitamins, hormones, and other biologically active agents, often used because they are believed to be beneficial. Also, one cannot ignore the importance of physical agents, such as actinic rays, which have profound effects upon the skin. One of the more poorly appreciated facts is that there are enormous species differences in the anatomy, physiology, and chemistry of the skin. The skin of different animals often responds differently to chemical and physical agents.

This focuses attention on the most important responsibilities of the investigator of skin, who must design his experiments in such ways that his results are valid and intelligible. One cannot read experimental results when one is not familiar with the various expressions of normality of the skin of the experimental animal used. These are some of the practical problems of the cosmetic chemist, as they are the fundamental problems of the biologist. Some of the problems of the biological investigator will be discussed, and specific examples will be cited which have a bearing upon the elucidation of basic biological phenomena, as well as a bearing upon the problems of maintaining the health of the skin, protecting it and making it more attractive.

New Methods for the Study of Percutaneous Adsorption

Kenneth M. Wilson
U. S. Army Chemical Research and Development Laboratories

Because of the complex nature of living skin, the diffusion of substances through it must often be measured by methods different from those applicable to thin, inert membranes.

In recent years new and sensitive techniques have been devised to study skin penetration and include radio isotopic tracer methods applied to both isolated skin and skin "in situ". These methods will be described and a technique of preparing a perfused skin flap will be illustrated by a color film.

Other techniques to be discussed will include the use of intradermal injection of substances giving an observable biological response and the use of model systems such as the cornea. Some aspects of the physical chemistry involved in skin penetration will be discussed briefly.

Methods of Appraisal for Potential Hazard

Adolph Rostenberg, Jr., M.D.
Department of Dermatology, University of Illinois, College of Medicine

The potential hazard of cosmetics can be divided into two major categories: (a) systemic, and (b) local. Systemic hazards can be acute or chronic. Local reactions can be subdivided according to whether they involve the skin or mucous membranes. In turn, each of these can be classified according to whether they are acute or chronic. Somewhat different testing procedures are employed to determine potential irritation for mucous membranes and for skin. A consideration of various technics that are utilized for the detection of potential primary irritation will be given. Some of these are the rabbit eye technic, the repeated application to damaged skin, and the repeated patch test. Various technics for predicting the development of allergic sensitizations will be discussed. Some of the procedures to be discussed are: (1) the Landsteiner, (2) the Schwartz-Peck, (3) the Draize, (4) the Shelanski-Shelanski, (5) the Brunner-Smiljanic, (6) the Traub-Tusing-Spoor. A brief discussion will be given of the technical aspects of these tests and some consideration as to their respective merits. A final word on the statistical aspects of prediction will be given.

The Government's Role in the Control of Cosmetics

Irvin Kerlan, M.D.
Bureau of Medicine, Food and Drug Administration

Federal control of cosmetics under the Federal Food, Drug and Cosmetic Act serves to provide safe, truthfully and informatively labeled and unadulterated products. Basic requirements of the law are designed to afford public health and welfare safeguards for the consumer and the industry. Through continuing enforcement activities of the Food and Drug Administration, an approach is at hand to control the quality and purity of these regulated articles.

Scientific methods are used and, when necessary, methods are developed for analysis of products. Protection of users from actually or potentially dangerous cosmetics is a major area of control which necessitates extensive background data on dermal toxicity and the sound evaluation of such information.

The appropriate use of color additives in cosmetics has been widened in a new law which has recently been enacted to deal with all colors, including coal-tar colors, through batch certification where necessary and authorization of tolerances where necessary to ensure safe use of colors. It is essential that the carcinogenic properties of color additives be determined.

Cosmetic ingredients may undergo changes in final formulations or interact to form new substances. In the interest of the protection of the public health and welfare, each article that is applied to the body should be adequately pretested for safety before marketing. Additional legislation is needed to ensure this measure of safeguarding the public.

The addition of physiologically active substances to cosmetics requires continuous and active study to determine their fundamental properties relating to skin physiology, biochemistry, pharmacology, and toxicology. The addition of drugs to cosmetics represents a special area of interest to the industry as well as the consumer to ensure that such products are safe, honestly labeled, and free of adulteration.

Industry's Interest and Responsibility in Cosmetic Safety

Willard M. Bright
Lever Brothers Company

As the science of cosmetic formulation and evaluation has developed in recent years, industry has increasingly employed a wide variety of scientific techniques to evaluate both the efficacy and safety of new cosmetic products. New and more informative analytical methods are used to insure the purity and reproducibility of raw materials going into cosmetic products. Improved techniques are being applied in evaluating the effects of new products on the skin. For example, percutaneous absorption is being studied with improved histological techniques and radio tracer methods. Enzymological methods of assaying

the effects of cosmetics on skin and physical chemical measurements in studying the kinetics and energetics of cosmetic effects are becoming more important. These developments have led to a closer relationship between fundamental research and product development.

Many straightforward techniques are available both with animal studies and with human volunteers for studying primary irritation but the problem of allergenic dermatitis is still not well understood. However, some progress has been made in the development of hypoallergenic products. Industry is working closely with dermatologists and commercial research laboratories, and with scientists in universities and governmental regulatory agencies, in a program of advancing the science of cosmetic formulation.

The Clinical Dermatologist and Cosmetic Reactions

Howard T. Behrman, M.D.

In the over-all picture of active dermatologic practice, a certain percentage of skin reactions due to cosmetics is encountered. In this report, an attempt is made to delineate the types of reactions, the frequency of their occurrence, the causal mechanisms, clinical features, differential diagnosis and therapy of these skin manifestations. The lecture will be illustrated with colored slides of the different entities.

The Science of Safe Cosmetic Formulation

Glen J. Sperandio, Ph.D.
Purdue University, School of Pharmacy

The art of formulating cosmetics has, in recent years, advanced to such an extent that it has become a science, and a highly specialized one. Of greatest concern to the cosmetic scientist is the question of the safety of his formulations.

A "safe cosmetic" can be achieved only after consideration of a number of various factors. These factors, as well as the actual components themselves, are discussed. It is shown that in establishing formulations the interpretation and utilization of data from other disciplines has become a necessity; the role of every division of a cosmetics house in contributing to the ultimate safety of a product is equally significant.

The characteristics and qualifications of the "ideal" man for cosmetic formulation point to the cosmetic pharmacist, whose academic training embraces both scientific and technical aspects of formulation; but an essential quality of all who are engaged in formulation studies is originality. As an example, new concepts of formulation are suggested. The use of food stuffs as cosmetic ingredients may be greatly increased. The problem of modifying formulas to conform to new governmental regulations is reviewed and possible future formulation techniques are considered.

Dermatologic Research and Cosmetic Formulation

Allan L. Lorincz, M.D.
School of Medicine, University of Chicago

Although it would seem almost axiomatic that dermatologic research should play a fundamental role in cosmetic formulation, relatively little direct support for such research has so far been provided by the cosmetic industry and the potential benefits that dermatologic research can bring to the field are still largely untapped.

A number of examples can already be cited of the great influence which dermatologic research has had on cosmetic formulation. Often this research has been soundly applied by the cosmetic industry to produce cosmetics which are both effective and harmless. Unfortunately, however, such research findings on occasion have been also unsoundly or prematurely applied to cosmetic formulation resulting in products which at best fail to measure up to the claims made for them and which may even be harmful.

Several outstanding illustrations of the sound application of dermatologic research to cosmetic formulation can be cited such as Blank's classic studies on the important role played by hydration in maintaining the softness and pliability of keratin which has much influenced the formulation of emollient preparations. Basic dermatologic research on sunburning and suntanning has likewise been very effectively applied in the formulation of sun-protective and suntan-permitting preparations. A large fund of dermatologic experience with, and basic research on, cutaneous irritants, allergic sensitizers, and percutaneous absorption has also been usefully applied by the cosmetic industry.

Many of the misapplications of dermatologic research have involved the use of hormones, antibiotics, and vitamins in cosmetic preparations. Examples will be cited of these and other instances where promotional or other considerations have apparently outweighed scientific evidence in cosmetic formulation.

Radioisotopes in Cosmetic Research

William F. Bousquet
Bionucleonics Department, Purdue University

Radioisotopes provide a most sensitive and precise tool for the research scientist. The development of radioisotope tracer techniques and methodology has opened new areas of research endeavor to the chemist and biologist.

In the fields of cosmetic formulation and evaluation the availability of radioisotopes and isotopically labeled compounds, as tracer substances, allows a more scientific approach to the various problems encountered.

Since the advent of the Food Additives Amendment, the cosmetic scientist is called upon to furnish detailed proof that ingredients in his products are not toxic and/or are not absorbed into the general circulation. This requires him to have at hand the most sensitive chemical analytical and bioassay procedures available. Radioisotopes, to date, provide the best analytical approach to studies of this nature.

This paper presents a brief discussion of the general properties and characteristics of radioactive isotopes, and points out areas where, in the author's opinion, isotope methods and techniques should prove valuable to the cosmetic scientist and manufacturer.

This is the third and final installment of a chronological account of the tour by members of the Society of Cosmetic Chemists of the U.S. through Europe last summer.

With the SCC tour—by Maison G. deNavarre

Among those awaiting us at the Barcelona Airport were Dr. José Artigas, Carlos Susanna, Juan and Ramon Visa. It was slowly getting dark. My girls went along with young Ramon Visa while Jeanette and I drove into town with Senior. The others came by bus. My family and I put up at the Avenida Palace while the others stayed at the pleasant Colon.

The Spanish S.C.C. held an informal reception in one of the lounges at the University of Barcelona. Their members and wives were all there by the time of our arrival. Although a goodly number of the members were known to me, they were strangers to most of our group. Noble sherries and rich amber malagas tantalized our palates to the desired edge for dinner.

At 8:30 p.m. about a dozen of us took off toward the harbor area. A Yankee aircraft carrier was in port and so were the hundreds of its crew. Our destination was the famous Los Caracoles (Snail) dating back to 1835 and presently operated by portly and DeGaulle-nosed Senor Bofarull who apparently eats at his own place. The restaurant is on a corner of two very narrow cobbled streets and narrow sidewalks. On the very corner is a grand outdoor spit on which a couple dozen chickens are broiling continually.

The cuisine is Spanish. Only the very hungry come here. Sea foods from angulas to zarauela are on the menu along with such Yankee specialties as Bistec or Salomillo, pallo and Lomo, all con patatas. The Bullabesa (Bouillabaisse) here is said to be tops—I must come for lunch sometime. Most of the group had Langostinos; Jeanette ordered Langosta; Pallo (Chicken) from the Rotiserie was for me. We had a very nice bottle of Perelada Blanco, 1954, that gave the food just the right flavor.

Vice president of Barcelona Province Dn. Antonio Ferrer-Pi, greeting Dr. Jose Artigas representing the IFSCC tour at a reception.

Ageing hams, cheeses, strings of garlic and peppers could be seen hanging from the ceiling in the Main Hall endowing the place with a characteristic atmosphere. The dozen dining rooms were jammed. Mrs. Susanna mentioned that the owner would be checking up on our food and service and indeed he did appear, all of him.

Perhaps Spanish brandies don't compare with those of France for example, but later we enjoyed some at a sidewalk café as a night cap.

The next day, Tuesday, September 6, the Sociedad Española de Quimicos Cosmeticos international seminar at the University was held in one of the Chemistry Amphitheaters. We were a small group, a bit fewer than fifty, but we were all deeply interested in the six papers to be presented.

S.C.C. president, Jerry Amsterdam, presented for the benefit of the Spanish audience, the Conrad, Motiuk and Maso paper on the resistance to hydrolysis of acetelated lanolin derivatives. Here I must interrupt to mention a feat I had not seen performed. Dr. Enrique Casassas of the University Chemistry Staff translated directly into Spanish without hesitating back-tracking or committing a solecism, all the English manuscripts, just as if they were written in Spanish and vice versa. We were all fascinated by his bilingual ability.

José Pascual (Surfoc, S.A.) then gave a paper discussing the various factors influencing the emulsifying properties of different PEG 400 monooleates.

The chromatographic identification of the main watersoluble azocolors in the food, drug and cosmetic industry was a paper authored by José M. Pla. C. Fauli and A. del Pozo, all of the Faculty of the College of Pharmacy.

By special arrangement, the paper by Mary Nebel and me, reviewing the application of the Infracord 137 to product control, was given in Spanish. The slides, really the most important part of the work, were to be discussed by me in English. On the third slide, the projector bulb actually exploded—and that was that for all succeeding projections.

Dr. José Artigas in conjunction with F. Buscarons and C. Rodriguez-Roda, all from the University Science Faculty presented a new colorimetric application of the ferricyanide-orthodianisidine system in relationship to the determination of cystine. The lack of a projector did not prevent Dr. Artigas from using blackboard sketches to establish his points.

A. Bodrinas gave the last paper on the use of sequestering agents in stabilizing Vitamin C. He found diethylenetriamine pentaacetic acid as being much superior to E.D.T.A.

At the close of the session Dr. Artigas introduced me to the rector of the University in castle-like quarters, with red velvet drapes, beautiful paintings all embellished with nut brown wood paneling. The rector was a dignified gentleman who reminded me of the grandees of Spain I had seen in pictures.

Now to the Palace of the President of the Province of Barcelona for a formal reception and pictures. Speeches in Spanish and English. Richly flavoured aperitifs and zestful canapes gave us the chance to literally absorb the beauty of the paintings, gold leaf

At the reception for SCC members in Barcelona

and over-all resplendant and regal atmosphere. We toured the palace, saw the special state meeting rooms and all the finery in which gold and silver played a dominant role.

The entire party went back to the Colon for lunch from whence many went on the city tour.

Senor Juan Visa and son Ramon picked us up for a visit to the Spanish Village. This place has authentic homes, shops and streets from each of the Spanish provinces. The effect is quite striking. Largely a tourists' spot, there are a lot of unusual sights such as glass blowing by old artisans, lace making, painting, brazing and iron works—and of course pastry and wine shops. We picked up a tasty morsel to munch on as we walked, called a Churo, a long stick-like, deep fried pastry covered with powdered sugar. It was hot, and literally melted in your mouth. The girls found interesting shawls while my eye was attracted by a goatskin wine bag—something everyone needs, especially at a bull fight.

The grand banquet that night was held in an outdoor place called la Masia. There are two places with this name. The one we were at was in the suburbs via Avenida Generalisimo Franco. The tables were set in a clear area to the left of the dance floor, surrounded by tall straight pine trees. The sky, full of stars and a moon to one side, looked down on the largest gathering of members, wives and guests the Spanish S.C.C. ever had. Indirect lighting and candles gave the feeling of isolation and closeness.

Aperitifs with the traditional sherry in both abundance and excellence. I tried a cock-sherry and gin —which someone suggested. About 10:00 p.m. we sat down to a dinner of the following:

Crema de Esparragos
Filetes de Lenguado Romana
Salsa Tartara
Medio Pallito al Asador
Verduras del Tiempo
Biscuit Glace al Chantilly
Moka
Vinos Blanco y Tinto
Aqua Mineral
Licores Finos

The sole in particular leaves a pleasant memory for as many who know me know that foods from the sea and I do not get along. The Romano sauce was especially gustful.

If you know only a bit of Spanish, you will agree that this was truly a banquet. Our wines were a delicate Marfil, which is a white wine, not too dry, and a Cune Rioja Clarete. Sra. Susanna was my right hand dinner partner. We recounted our previous meeting on the boat ride on the Rhine when we were all guests of the German S.C.C.

And then the dance music started. Two orchestras, alternating between Latin and all the other dance tunes known the world over.

Between dance tunes, President Amsterdam made a presentation of Lenox China to Dr. Artigas on behalf of the tour group in appreciation for all their hospitality.

After a few dances on a glass floor illuminated

with blue and green light from underneath, we left our two youngsters in care of the Susannas to be brought home when the older people left. Between my two teen agers and the three other unattached ladies in our party, the Spanish group in which the men outnumbered the women, had a ball. Although too often there was a language barrier, music was a common bond of fun and friendship.

A bit of shopping on the Paseo de Gracia, and the Avenida José Antonio we equalized the trade balance at Loewes' which shop specialized in leather.

The Visas, father and son, met us for a quick drive around the city and then to lunch at an interesting Basque restaurant called the Guria. It is a combined sidewalk and inside restaurant. First a Tio Pepe, then the meal itself. Ramon Visa took the two young ladies under his direction. As an appetizer, a Spanish tortilla (with potatoes) was practically a meal in itself. In the Latin countries, lunch is the main meal starting about 2:00 p.m. and lasts a couple of hours.

A bottle of Peralada Rojo, 1952, helped with the Cochinillo (roast young pig). The girls who couldn't afford the calories any more than I, couldn't refuse the Flan, a molded custard dessert.

Sr. Visa, our host, is managing director of the company who manufacture the Floid line of men's toiletries. He drove us to their new plant which is truly a beauty inside. The plant had only recently been occupied and all the housekeeping was not yet complete. But we were all greatly impressed with the brightness and cleanliness, the pink and white marble so effectively used as well as the spacious and well appointed offices.

By now it was time to leave for the airport where the rest of the group would be awaiting us. Indeed they were, along with a delegation from the Spanish S.C.C. At 6:30 p.m., we boarded Iberia Flight 303, arriving at Madrid a bit after eight.

At the new Carleton Hotel, presumably air conditioned—at least some rooms were, but not ours, we were able to go to our rooms, unpack and just make dinner comfortably around 10:00 p.m. The food here is not outstanding but it is quite acceptable.

Our first day in Madrid, we toured the city via the Avenida José Antonio, Plaza Espana, the Castle Palacio Real, Plaza Mayor, Puerta del Sol, Del Prado Museum and back to the Hotel. At the Castle we saw the beautifully maintained rooms, including the dining room where Franco gives dinner parties with food brought in from the Ritz Hotel.

Everyone was dazzled by the Prado museum with its paintings by Goya, El Greco, Murillo, and Velazquez. Indeed, I was quite amazed at the realism in Goya's famous "Nude Duchess" which is a painting some 3 x 5 feet along with its "dressed" counterpart painted within 24 hours after the Duke saw the original.

Sadness, unhappiness, poverty all verging on despondency are nowhere more exemplified than by the Spanish painters. It is said that it was their way of telling the world of the afflictions of their people at the time.

A little more shopping in the afternoon. At night, *after* dinner, we all went to the Zambra, a Flamenco cabaret where the "pure, unspoiled folk-art of Andalusia" is revived and maintained. Spanish brandy on the rocks with a touch of soda helps to understand what goes on in front of you. The Flamenco troupe is composed of male and female singers and dancers, guitarists and "jaleadores" who clap a rhythm. It's a bit noisy in the front row as we were, but if you can find the inner rhythm or "son", it takes on greater meaning.

With the SCC tour in Lisbon; above, Bart Owel, Mrs. Edison, Dr. Edison, Jeanette deNavarre and August Baumeister; below, Kurt Pfeiffer, M. G. deNavarre, Dr. Sophie Plechner, August Baumeister, Jerry Amsterdam and Nelson A. A. Soromenho.

The following morning, we were off for Toledo, some 70 kilometers Southwest from Madrid. The road is either brick or stone, (feels like large stones when riding the wheels on the bus). It takes well over an hour to get there through fairly barren country.

Toledo, once a Spanish capitol, is one of the oldest cities in Europe. It is strategically located high on a rocky hill, practically surrounded by the Tagus River. The city's architecture reflects the changing occupation and social times such as the Moorish, Renaissance and Gothic. One building definitely Moorish, was also a synagogue and a Catholic church. In this city at the top of one of the lower hills, is the El Greco museum, formerly his home. At the Church of Santo Tome, one can see the famous El Greco painting "The Burial of the Count of Orgaz". The city is

largely surrounded still by a heavy wall both Moorish and Gothic in style. Unfortunately, we did not visit the Alcazar which figured so much during the Civil War in 1936.

We lunched in a lovely spot, high in the hills on the outskirts of the city called the Cigarrol Hotel Monte Rey. The view into the valley below was breathtaking.

No visit to Toledo is complete without a stop at the government armory producing the famous Toledo steel products. It is a great demonstration, running a dagger through a sheet of iron, without damage to the dagger. This industry was brought to the Iberian peninsula by the Moors hundreds of years ago.

Our tour was slowly coming to an end. We had lost a number of people enroute who had to get their children back to school. So, on Saturday morning we paid up our bills for extras at the Carleton and bid good-bye to the Paseo Delicias and Madrid, to go via Portuguese Airlines Flight 551 for Lisbon.

Kurt Pfeiffer met us at the airport to tell us that his superior at Tokalon, August Baumeister who was in town, had organized a dinner party at the Falclore Restaurante for the group. This was indeed a very gracious offer and we were happy to accept on our last night in Europe.

We arrived in time to go to our rooms at the Embaixador Hotel and prepare for lunch. A little shopping—a bit of rest, then we got ready for dinner. The last time I had seen him, Mr. Baumeister, was in Paris in June. He looked hale indeed. Jeanette hadn't seen him since our first trip over in 1956.

The Falclore is a cabaret type dining room, serving excellent food and presenting Portuguese folk songs and dances. Many ordered soup and steak. Being only slightly venturesome, I tried the canja de Galinka (chicken soup), Linguado Margarida (Sole), Figadode Vitela Portuguesa (Veal), Campata de Fruta, cafe and a number of bottles of Mateus Rose, a local wine which is bottled in amber glass. It is faintly carbonated, reminding us of the Doles of Switzerland.

The entertainment was extraordinarily good. Indeed we saw two of the shows. By now it was past midnight and time to thank our host and bid him good-bye.

We hardly arrived at the hotel when all the lights went out until the next morning.

It was but a short walk to church the next day, Sunday. I was quite surprised by the number of widows attending mass.

The Embaxiador dining room is on the top floor of the hotel and what a panoramic sight while eating. The service is absolutely perfect. The food is of the best. Our last meal here was lunch. We boarded our bus for the airport directly from it.

Pan American Flight 155 left Lisbon a bit late, but arrived at Idlewild about 7:45 p.m. after a one hour stop in the Azores. Going through customs was a madhouse. We were lucky enough to get an American Airline Flight at 9:00 p.m. We rushed from Idlewild to La Guardia and there bumped into F.D.A.'s Bob Clarke—a wave of the hand and we made our flight in the nick of time.

All is well that ends well.

Tweens. Contribution to the Knowledge of Solubilization by Tweens by St. Ello (Ungaris che Pharmakopoekomission, Budapest, Hungary).

Almost empirical data only has been published about the quantity of Tweens to be used for the solubilization of various aqueous soluble materials. The author tried to comprehend the very complex question by using the relation material: Tween by aqueous titration (cloud point) and to register the results graphically. He used volatile oils such as peppermint, fennel and cassi-cinnamon, as the substances to be solubilized. He tested how much Tween 20, 40, 60 and 80 is required for the solubilization of increasing quantities of the volatile oils, resp. with what quantity of water in different oil: Tween relations the cloud point is reached. *Thru Am. J. Hosp. Pharmacy, 17, 311 (1960).*

Quantitative Evaluation of Granulation Tissue in Experimental Wounds.

A method has been devised permitting quantitative evaluation of the granulation tissue formed in experimental wounds: Plastic rings are incorporated into the wounds inhibiting contraction of the wound edges and epithelization of the wound. The rings also induce regular growth of the granulation tissue. By this method it was possible to demonstrate that the growth of granulation tissue is inhibited by hydrocortisone, 3, 5-dioxo-1, 2-diphenyl-4-n-butylpyrazolidine (Butazolidin) and sodium salicylate in proportion with the dose applied. This method is recommended to test drugs which influence wound healing. *Thru Arzneimittel-Forschung, April, 1960, p. 228. By Von Barbara Rudas.*

Paraphenylenediamine Sensitivity.

"A number of amines used as rubber antioxidants were patch tested for evidence of cross sensitization with PPD. A history of systemic drug reactions appeared to be a determinate factor. In the absence of these, the amines were tolerated without incident; but where there had been systemic reactions from procaine, sulfonamides and penicillin (procaine), positive patch tests developed to butyraldehyde aniline condensation product and 2, 4-toluene diamine. These reactions reproduced the intensity of the previous reaction to PPD. The findings suggested that a positive patch test to PPD might indicate a sensitivity of one or more types: 1) epidermal and/or eczematous sensitivity alone, 2) combined epidermal and systemic sensitivity occurring from previous drug reactions. The latter one was the type in which possible cross reactions to the amines occurred. A positive patch test to PPD is a clinical indication of possible rubber sensitivity." I. Edward Gaul. *Thru J. Invest. Dermatology, April, 1960, 34 (4), 258.*

Cloud Point as a Means of Characterizing the Polyglycols of Polyoxyethylene (8) Stearate by M. D. Brewster and J. D. Brandner, Atlas Powder Co., Wilmington, Del.

Polyoxethylene (8) stearate which has been used extensively in yeast-raised baked goods may be characterized by the cloud point of the recovered polyethylene glycols. This test is sensitive to the molecular weight distribution of the polyglycols in the mixture and hence will distinguish between polyethylene glycols which have a Poisson-type distribution and those of the same average molecular weight but having nonrandom distribution of polyethylene glycols. Cloud point is particularly sensitive to the presence of polyethylene glycols of molecular weight greater than 600. *Thru Agri. & Food Chem., May, 348(1958).*

Studies on the Spreading Test of Skin Tallows. G. Hopf and A. Winkler (General Hospital, Heidelberg). Fette Seifen Anstrichmittel 61, 974-77 (1959).

Measurements of the skin fats in the region of the capillitium with the aid of the spreading test gave different values in different age groups. Surface active free fatty acids were responsible for the workability of the spreading test. The conclusions reached were based on the observations of the unchanged tallow, which has not been acted upon by esterases, e.g., in tallow cysts and in the deeper regions of the comedones possess very low spreading values. On the other hand, the spreading values are higher in the upperparts of comedones because of the presence of free fatty acids. *Thru J. Am. Oil Chemists' Soc., 37, 201 (1960.)*

U.S. No. 2,927,052. Process of Producing Oligodynamic Metal Biocides, patented by Zdenek Vaclav Moudry, Northfield, Ill., assignor to United States Movidyn Corp., a corporation of Illinois.

The patent teaches the process of producing oligodynamic metal microbicides comprising forming an aqueous solution of a water soluble oligodynamic metal salt containing a colloid stabilizing proportion of an ionizable-halogen-free gelatin having a viscosity of 20-40 millipoises, an isoelectric point of pH 7.8-8.3 and a pH of 3-5 and irradiating said solution for from several seconds to one hour with actinic light having an intensity of at least about 45 milliwatts per square foot, at least 40% of the total radiation lying in the infrared portion of the spectrum, at least 25% of the total radiation lying in the ultraviolet portion of the spectrum and a material portion of the radiation being emitted at 3130-3660 A.U., and thereby producing a stable colloidal dispersion of oligodynamic metal microparticles predominantly smaller than 200 A.U. *Thru Soap and Chem. Specialties, June, 1960, p. 159.*

Diagnosis and Management of Hirsutism

By Howard T. Behrman

(Digested from the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION Vol. 172, No. 17, p. 120/1924.)

Hirsutism or hypertrichosis, as described in The Journal of the American Medical Association, is a relative term used to indicate the presence of excessive hair on various body surfaces which normally grow hair or the presence of hair in normally hairless areas. There have been numerous attempts to classify hirsutism and its causative mechanism. Idiopathic hirsutism is probably the commonest grouping in women. The tendency toward this type of hirsutism may be familial and often appears

in women of Mediterranean origin. Previously, it was thought that there were no specific metabolic, chemical, or endocrine changes in this disorder, but recent studies showed that moderately elevated quantities of urinary 17-ketosteroids were excreted by women with this condition. Some investigators used cortisone therapy to decrease steroid excretions to normal values, but Kappas and Perloff concluded that hirsutism of the type discussed was due to primary changes in the adrenals. Physiological hirsutism applies to the excessive growth of hair during the periods of puberty, pregnancy, and the menopause. The causative mechanisms are probably adreno-cortical in origin, although gonadal and pituitary factors also play a role. Therapeutic hirsutism can be exhibited by the administration of testicular hormones to women, in sufficient dosage and for a long period of time, with the result of defeminization. Similar effects have been observed after the administration of large amounts of cortisone and adrenocorticotropin. Miscellaneous causes of hirsutism include congenital ectodermal dysplasia, mumps, encephalitis, certain types of neuritis, and multiple sclerrosis.

Major endocrine changes of adrenal origin may result in the development of two syndromes characterized by hirsutism-adrenogenital syndrome caused by a tumor of the adrenal cortex and Cushing's syndrome due to an increased secretion of hydrocortisone and its derivatives. Hirsutism is seen in patients with the occurrence of masculinizing ovarian tumors and in patients with ovarian dysfunction. The result is the Cushing's syndrome and the Stein-Leventhal syndrome. Hirsutism of the pituitary origin is due to a basophilic adenoma of the anterior lobe of the pituitary gland. Other causes of hirsutism include testicular tumors, juvenile hypothyroidism, malignant thymomas, pancreatic carcinoma, and other uncommon entities.

Assay for Bithional in Liquid Soaps

By Jean B. Matuszak, Frank W. Bope and Lloyd E. Harris

(*Digested from DRUG STANDARDS, Vol. 28, No. 3, May-June, 1960, p. 68.*)

A spectrophotometric method for the assay for bithionol in liquid soaps was described in the publication, Drug Standards. The results obtained by this method were compared to the results obtained by using a procedure proposed by Van Der Pol. Other procedures used either gave unreliable results due to the fleeting colors produced using colorimetric techniques or required several extraction steps to be taken. The procedure used by the authors is a modification of the differential spectrophotometric method for hexachlorophene developed by Childs and Parks, referred to as the "differential method", by using buffer solutions. The formula used in the calculation was:

$$\% \text{ Bithionol} = \frac{D \times 10^6}{376 \times G}$$

where D = measured extinction at 328 mμ.
and G = weight of sample in gm.

Potentiometric titrations determined that an acid reagent such as a hydrochloric acid solution, 0.5 N in 90 per cent methanol, insures suppression of ionization of bithionol in the presence of soap, and there is no need to add a base to produce a pH of 8 for the more alkaline solutions since a 90 per cent methanol solution of 500 mg./100 ml. of soap base and containing as much as 6 mg./100 ml. of bithionol has a pH very close to 8.

Isobutyl Linalool for sweetness —

Isobutyl Linalool, a new patented homolog of Linalool. Not to be confused with Linalyl Isobutyrate. Gives natural sweetness to any compound. Particularly suitable for light florals. Stable: does not discolor. Available through principal essential oil dealers.

Aromatics Division

HOFFMANN-LA ROCHE INC · NUTLEY 10 · N. J.

NOrth 7-5000 · N. Y. C. - OXford 5-1400

Also new—

Isobutyl Heptenone

fruity,

powerful

ketone

* * *

stable -

does not

discolor

Aromatics Division

HOFFMANN-LA ROCHE INC · NUTLEY 10 · N. J.

NOrth 7-5000 · N. Y. C. - OXford 5-1400

Bithionol was found to absorb to a different extent in the presence of each of the soap bases used in this study.

A standard bithionol graph was made by comparing a pH 2 series of aliquots to a pH 8 series of aliquots. The pH 2 member was placed in the solvent cell and the pH 8 members in the solute cell of the spectrophotometer. The series were arranged in pairs of the same concentration. The observed absorbance was plotted at 328 mu, slit width 0.09, on the ordinate scale against the corresponding concentration on the abscissa scale to give a straight line passing through the origin. The sample of bithionol liquid soap was prepared similarly to the standard solutions by weighing 5 gms. of the liquid soap into a 100 ml. volumetric flask and diluting to the mark with 90 per cent methanol. To each of two 50 ml. volumetric flasks, 5 ml. of this biothionol-soap solution was added. One was filled with 0.5 N methanolic hydrochloric acid and the other with 90 per cent methanol. The former solution should have a pH of 2 and the latter a pH of 8. The two were compared in the spectrophotometer at 328 mu and with the aid of the standard bithionol graph, the mgs./100 ml. of bithionol in the aliquot of soap were determined. The calculation is as follows:

$$\% \text{ Bithionol} = \frac{\text{mg. bithionol/100 ml.}}{\text{sample wgt. in mg. x (5/100) x 2}} \times 100$$

The results of the series of assays by this procedure gave mean ± standard deviation of 99.4 ± 1.6 based on the per cent of the labeled amount found. Van Der Pol's procedure produced a mean ± standard deviation of 97.7 ± 3.5. Each of the values found were the result of three or more determinations with a standard deviation of ± 0.01 for each figure. Using this standard deviation it was calculated that the standard deviation expressed in mg. would not be more than ± 0.0006 mg. per 100 ml. which quantity is not measurable by the methods used. If either of the two procedures had been used, the standard deviation would be much larger but still not appreciable. It is then reasonable to assume that the proposed procedure is accurate and precise.

Quantitive Determination of Ethanol in Pharmaceutical Products by Gas Chromatography

By Harold J. Wesselman

(Digested from the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, Vol. 49, No. 5, May 1960, p. 320.)

The time consuming distillation method described in the U.S.P. XV could be discouraging to the chemist having many ethanol preparations to assay. A successful application of gas chromatography has been suggested in the May issue of the Journal of the American Pharmaceutical Association which allows samples to be assayed with little or no treatment in a short time with equal or better accuracy. It was found experimentally that polyethylene glycol 400 was a suitable stationary phase because it resolves ethanol, water, and acetone completely. Since the accuracy of the direct measurement of peak heights for quantitative determinations of ethanol depends mainly on the ability to inject accurate volumes of samples, the internal standard technique of Ray (1) was used and acetone was selected as the best internal standard. Thus, the acetone was added to the sample in a known proportion, and the peak height of the ethanol was referred to the peak height of the internal standard. Calibration curves were obtained by measuring the ratio of the peak heights of ethanol and the internal standard, and this ratio was plotted against the percentage of ethanol. Standard solutions containing acetone and a suitable amount of ethanol were prepared for each sample to be assayed. The sample was diluted with the same amount of acetone that was contained in the standards. These samples and standards were then chromatographed with the Podbielniak Chromacon using 30% (w/w) polyethylene glycol 400 using helium as the carrier gas. The peak heights of the acetone and ethanol were measured accurately and the ratios calculated and plotted against the concentration of ethanol. From the standard plot the concentration of ethanol in the dilution with acetone gave the amount of ethanol present in the original sample. Comparisons obtained from tests done on fluid extracts, elixirs, tinctures and other products exhibited satisfactory results.

(1) Ray N. H., J. Appl. Chem., 4, 21 (1954).

Antimicrobial Properties of Dodecyl-Di (p-Hydroxyethyl)-Benzyl-Ammoniumchlorid.

The range of action comprises gram-positive and gram-negative bacteria, pathogenic yeast organisms and dermatophytes. The substance possesses favourable emulgation and solution properties towards substances sparingly soluble in water. The excellent skin tolerability shown in experiments is confirmed in several thousand persons by application of dermatological cosmetical preparations without side-effects over a period of years. The a.m. properties, especially the marked action against staphylococci and dermatophytes recommend the use of D 301 not only for the purpose of disinfection, but moreover for therapeutical application in certain fields of medicine, especially dermatology. *Thru Arzneimittl-Forschung 10, pg. 625.*

Lipoperoxides and the Hair Follicle. P. Puig Muset, J. Martin, N. Fernandez, J. Valls.

In previous studies of one of the authors, we have commented on the possible importance which the peroxides, their derivatives of radical structure and their combinations with lipids may have for the physiopathology of the animal organism and especially its central nervous system. For this study we have used the lipoxidase enzyme as a means to generate a lipoperoxide hyperproduction in the treated organism and to analyze their reactions. In protracted treatment by oral administration, we observe after 40 days, a profuse loss of hair, with scopic examination shows atrophied hair follicles.

If lipoxidase is topically applied, no dermic action is observed, but if the enzyme is applied as a mixture with linoleic acid, alopecia of the treated zone is observed after a few days. Following intradermal injection of both the compounds, alopecia is observed after about fifteen days, at the same time, an ulcerative lesion appears. It is considered that this alopecia is due to the formation of lipoperoxides, which if accumulated, exert a toxic action on the hair follicle. The possibility is discussed that this mechanism may be of physio-pathological import.

Knowing from other studies that some substances are capable of inhibiting the formation of lipoperoxides, investigations are conducted to ascertain if some of these are capable to inhibit the onset of atrophy of the follicle and favour its regeneration.

In some preliminary clinical trials using N-phthalyl glutamimide per os and topically applied, good results are observed in cases of Alopecia areata. Further studies are in progress. *Thru Arzneimittel-Forschung, April, 1960, P. 234-238.*

PACKAGING & PROMOTION

1

2

3

1—Campana

Campana Corporation has introduced a new graceful bottle and an attractive foil label of Italian Balm, a hand lotion produced since 1926.

The company also has discarded the use of the familiar green and white checkerboard folding carton to meet the present trend to eliminate cartons which hide the package. However, miniature replicas of the carton are being affixed to the neck of the new bottles during an introductory period. Reverse side of tags state "We've had our face lifted! Like our new look? No carton—but the same fine original Italian Balm."

2—Bourjois

Bourjois, Inc. has announced the introduction of a new product, the Evening in Paris Cream Deodorant. Like the line's previously established "Roll-R" Lotion Deodorant and Stick Deodorant, the Evening in Paris Cream Deodorant will be packed two of a kind to an individual boot.

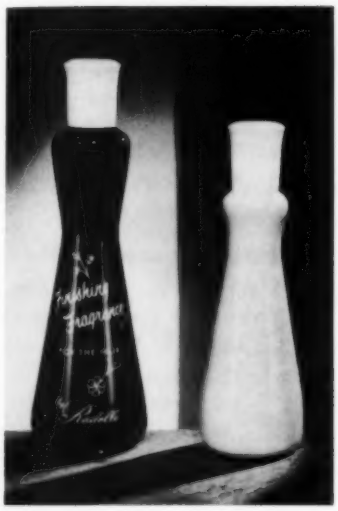
In presentation, the Cream Deodorant continues the Bourjois trend toward a more advanced concept in packaging design. With a narrow base and cap line, the jar accentuation revolves around an emphatic, middle band of content width. It is modern in every detail from the gracefully sloping sides to the heightened blue of the label and cap.

3—Noxzema

Noxzema has announced the introduction of new medicated makeup products—Cover Girl Liquid Makeup and Cover Girl pressed powder containing Noxzema medication built in. Both come in three shades: Light, Medium and Dark. The powder comes in three compacts, White, "Tortoise" and Black, richly decorated with a golden monogram design on the cover. The makeup comes in a tapered 1-ounce bottle with a golden cap and gold-and-white label.

4—Radelle

Radelle, division of Commercial Laboratories, Inc., have introduced two new scented deodorants, Finishing Fragrance and Spring Flowers, in glass pressure packages. Finishing Fragrance, a deodorant for the hair, is packaged in a shimmering black-sheathed glass bottle decorated with white screening. Spring Flowers, a cologne deodorant, is packed in a bottle covered with a delicate pink plastic, and decorated with white screening. Both packages are topped with white plastic closures. Products are delivered through the mail following "party-plan" solicitation.



4

5

6

5—Prince Matchabelli

Prince Matchabelli Inc., has introduced Polyderm Moisturing Lotion as the liquid form of Polyderm Compensating Cream, Prince Matchabelli's cosmetic treatment for dry skin. It contains the same three "essential polyunsaturates," known to be components of the healthy, youthful skin.

Because more and more women today express a preference for the lotion-form application . . . and the younger ones downrightly demand it . . . Polyderm has been made available in both the cream and liquid forms.

6—Wrisley

Allen B. Wrisley Co. has introduced Sof' Lite Lemon Shampoo. Lemon additives long recognized as an ingredient to bring out natural highlights in every hair shade, have been added to the Sof' Lite formula.

The Wrisley easy-grip bottle contains a supermild, rich lather shampoo, developed for use in hardest water and yet rinses out quickly.

7

7—Lentheric

Lentheric introduces the new Red Lilac Cologne Mist, in an exquisite aerosol spray flacon. A round of crystal, accented by vertical golden bands, reveals the Lentheric golden fleurs de lis inside and between each band.

Atop the gold-plated fluted cap . . . the Lentheric Lion Seal in relief. The box incorporates the "wild" new Red Lilac design Lentheric has adopted for the new Toilet Water and Bath Powder packages.

8—Prince Matchabelli

Prince Matchabelli introduces Abano Dry Skin Treatment Bath Oil, to join the classic Abano Bath Oil which was introduced by Prince Matchabelli thirty years ago.

A handsome addition to a bathroom decor is the milk-glass bottle with panel insets of aqua, gold, and ultramarine tiles in a mosaic design patterned after drawings of baths popular in the days of the bath-loving Romans. A gold-crowned white seahorse, the identifying symbol of the Abano Line, is part of the mosaic design. The hexagonal white gift carton is similarly decorated.

8

News of the Societies of Cosmetic Chemists

U. S. Society

Presenting the 1960 Award of the Society of Cosmetic Chemists to Dr. Robert H. Marriott is Mr. H. J. Amsterdam the societies President. To the left of the recipient is Mr. Maison G. deNavarre, Chairman of the award committee, as well as, the Master of Ceremony and eulogist during the award dinner.

The Society of Cosmetic Chemists honored Dr. Robert Henry Marriott, F.R.I.C., at its Annual Dinner Dance on November 29, 1960 at the Hotel Biltmore. Dr. Marriott received the Society's 1960 Medal Award for his contribution to chemical research in the cosmetic industry.

Acting as Master of Ceremonies and Eulogist for the Medalist, Mr. Maison G. deNavarre, spoke of the work of Dr. Marriott and reviewed his personal and scientific accomplishments. The presentation of the award was made by Mr. H. J. Amsterdam, President of the Society. Mr. A. Herzka, addressed the Dinner on behalf of the British Society of Cosmetic Chemists, and expressed that group's appreciation for that honor bestowed upon one of its members.

During the evening, Dr. Sophie Plechner was installed as President for 1961, and Mr. Warren Dennis was introduced as President-elect for the year 1962. Robert A. Kramer and Lester Conrad were chosen to serve again as Secretary and Treasurer, respectively, and elected directors included Walter Edman, John Longfellow, William Mueller and Martin Rieger. Serving as Chairman of the Society's Executive Committee for 1961 will be Mr. H. J. Amsterdam, the retiring President.

Dr. Sophie Plechner, President 1961, addressing the annual award dinner.

New York Chapter

At the annual Presidents Night, Mr. H. J. Amsterdam installed the 1961 officers of the New York Chapter of the Society of Cosmetic Chemists. In a short ceremony the gavel was turned over to Dr. Saul Bell, chairman. Dr. Martin Katz, chairman-elect; Agnes Korte, secretary; and Robert J. Schiraldi, treasurer, assumed their new duties for the coming year.

Retiring chairman Dr. John M. Longfellow presented past chairman Theodore Ostrowski with a plaque in recognition of his years of service to the New York Chapter.

British Chapter

Professor Davies opened with an historical account of emulsions, the division of emulsions into oil-in-water and water-in-oil types depending upon the emulsifier used and the attempts to predict the type and stability formed. The Bancroft rule states that the phase in which the emulsifier is more soluble will be the external one. The inapplicability of the rule when the volume of the phase in which the agent was more soluble was very small, for example one per cent. Later came the adsorption theories of emulsion stability. Langmuir and Harkins postulated the existence of an oriented mono-molecular film with the polar groups oriented towards the water phase and the non-polar hydrocarbon chains towards the oil. Unfortunately exceptions to the theory were known. Griffin (U.S.A.) introduced the concept of H.L.B. that is, hydrophile-lipophile balance.

Professor Davies designed a machine for the study of emulsions at the inversion point.

Los Angeles Chapter

The new officers of the California Chapter of the Society of Cosmetic Chemists, to be installed at the meeting of January 30th, are, from left to right: Ben Kapp, treasurer; Oscar Scherr—chairman; Harry Mace—Chairman elect; Bill Stidston—secretary.

. . NEWS AND EVENTS . . . NEWS AND

The Realistic Company enters hair color field with Color-Kist

Color-Kist gives three separate and complete salon services at one time—shampoos, colors, and conditions the hair in a single operation. However, each of its triple benefits are reported as effective as though given individually. The color "takes" in five minutes; will deepen or blend in more, if preferred, when left on longer. The fact color will absolutely not rub off is another positive advantage cited by the manufacturer. It will last through several shampoos.

Realistic Color-Kist Shampoo is available in six basic "natural" hair shades, although many additional shade variations can easily be obtained by mixing. It is distributed in concentrate form for professional beauty trade use exclusively.

Chesebrough-Pond's Inc. acquires Worldwide Northam Warren Interests

Two venerable and respected families in the cosmetics, toiletries and proprietary fields were united through the acquisition, by 80-year-old Chesebrough-Pond's Inc., of the worldwide interest of 50-year-old Northam Warren organization, for an undisclosed amount of cash.

Northam Warren's major products include those sold under the brand names of Cutex, Odo-ro-no, and Peggy Sage. Chesebrough - Pond's principal lines consist of Vaseline brand products, Pond's creams and cosmetics, Prince Matchabelli perfumes, Pertussin cough and cold products, Aziza eye cosmetics, and Seaforth and Black Watch men's toiletries.

Like Chesebrough-Pond's products, the Northam Warren line is sold principally in drug, variety and food outlets at popular prices.

Rutgers receives grant from perfume industries

A grant of $5,000 from twelve perfume industries to Rutgers for the continuance of its two year evening program in "Perfumery and Essential Oils" has been announced.

The grant will not only subsidize this lecture-laboratory program at the Newark Extension Center but also will enable the Center to offer several new courses of interest to the perfumery industry.

This is the second occasion on which the perfume industry has provided funds to subsidize perfume courses at the University. Three years ago, a similar amount was advanced to launch instruction in Turpene Chemistry and later, other courses in the identification, compounding, and manufacture of synthetic and natural perfumery raw materials.

Contributors to the $5,000 grant are Fritzche Brothers, Inc., International Flavors and Fragrances, The Givaudan Corp., Firmenich and Company, George Lueders and Company, all of New York City; Schimmel and Company, Inc., of Newburgh, New York; Laboratories of Rutherford, Hoffman-Shulton, Inc., of Clifton, Trubek La-Roche of Nutley, Verona Pharmaceutical Corp. of Newark, Albert Verley Company of Linden, and Noville Essential Oil Company of North Bergen.

(left) Mr. Northam Warren, founder of the Worldwide Northam Warren interests; (center) Mr. Jerome A. Straka, president of Chesebrough-Pond's Inc., the acquiring company; (right) Mr. Northam Warren, Jr., president and chief executive officer of the Northam Warren subsidiary.

NBBMA meets Feb. 23-24.

The National Beauty & Barber Manufacturers' Association takes over the Hotel Statler Hilton in New York for a two day convention from 2 P. M. February 23rd, to noon, February 25. The workshop sessions on Friday are divided into three periods with a choice of two sessions during each period, and run from 9 A. M. to 12 P. M., from 1 P. M. to 3 P. M. and from 3 P. M. to 5 P. M. The 9 A. M. to 12 P. M. sessions give the membership a choice of sitting in on either "How to Sell Effectively Through Dealers' Salesmen" with Revlon's Frank Vella as moderator, or the "Role of The Product Manager: Use of Advertising and Sales Promotion Materials" with Bill McKowen of Realistic as moderator. The 1 P. M. to 3 P. M. sessions make available two investigative meetings. One is on the "Export Market: Problems and Procedures" with S. I. Schulman of Ar. Winarick as moderator and the other is on "Effective Product Promotion Methods for Beauty and Barber Manufacturers" with Robert Henrichs of La Maur as moderator. The 3 P. M. to 5 P. M. session has two meetings, one devoted to "Trade Shows: Problems and Solutions" with Ira Stuart Wilson of Halliwell as moderator and the other tackles the problem of "Marketing Research: Its Value in Planning Sales and Promotions' with Robert Hoffman of Revlon as moderator. On Saturday morning, following the breakfast meeting, the workshop summaries will be presented by Frank Schaider and Maurice King respectively.

As usual, following the breakfast session, the annual meeting of the National Beauty & Barber Manufacturers' Association will take place together with the election of a new president and a new board of directors.

The Chicago Perfumery, Soap and Extract Association, Inc. elected the following 1961 slate of officers and directors at its annual meeting. Treasurer—George C. Kolar, president of Kolar Laboratories, Inc. Vice President—Jack W. Baldwin, sales representative of Hazel-Atlas Glass Division. President—John P. Helfrich, president of Helfrich Laboratories, Inc. Secretary—Harold W. Jelly, president of Walter H. Jelly & Co., Inc.

Noxzema enters makeup market with Cover Girl

Cover Girl Pressed Powder and Cover Girl Liquid Makeup have been introduced by Noxzema Chemical Company. Cover Girl provides Liquid Makeup and Pressed Powder that not only measure up to fashion and beauty standards, but are medicated and antiseptic to help protect the skin and improve the complexion. A plus benefit in the Pressed Powder's medicated formula is its ability to inhibit bacteria build-up on the puff from three to nine times more effectively than any brand tested—a very important factor in keeping the skin bacteria and blemish free.

The three Cover Girl shades, Light, Medium and Dark, represent an ideal range to meet every complexion need. Figures show that although large cosmetic lines may include eight to twelve colors, three or four shades account for 80% of the business.

FD&C Red #1 now is Ext. D&C #15

Two months ago FD&C Red #1 was completely delisted for any use in foods, drugs and cosmetics. Recently, however, this same color has been listed as Ext. D&C #15, for use in cosmetics other than those applied to the lips and mucous membranes.

Program for the Societe Technique des Parfumeurs de France

The program for this group for the coming months is as follows:

February, a discussion on The Notion of Fixation in Perfumery, by a committee composed of three perfumers, E. P. Meunier, J. Hervelin, H. Robert, and R. Gonnon, with one chemist.

March, a lecture by Mr. Drapier on the subject of Plastic Packaging.

The specific questions to be discussed at the February meeting are being studied, with the view of collaboration between this societe and the American Society of Perfumers.

Parfums Lucien LeLong purchased by Mary Chess, Inc.

The worldwide rights of Parfums Lucien LeLong, Inc., have been purchased by Mary Chess, Inc., and affiliated companies. It will be operated as a wholly-owned subsidiary of Mary Chess, Inc.

This is the third recent acquisition by Mary Chess. Previously Parfums Schiaparelli, Inc., was added in 1958, and the Marie Earle Corp. in September, 1960.

D&O moves to new location

Dodge & Olcott, Inc., has moved its general offices and laboratories to: Manhattan Industrial Center, Seventy-five 9th Avenue, New York 11, N. Y.

These quarters, furnished with completely new and modern laboratories and facilities, represent one of the few moves of the company since it was established in 1798.

Walter N. Plaut

Walter N. Plaut has been named president and chief executive of Lehn & Fink Products Corporation succeeding his father Dr. Edward Plaut, who will continue as a director of the company.

William O. Machamer has been named field supervisor for the sales force of Allen B. Wrisley Company, Chicago soap and toiletries manufacturers.

Jeanne Richard has been promoted to manager of the franchising division of Dorothy Lamour, Inc. Miss Richard will set up franchises for the house-to-house sale of the company's products.

Eugene P. Grisanti

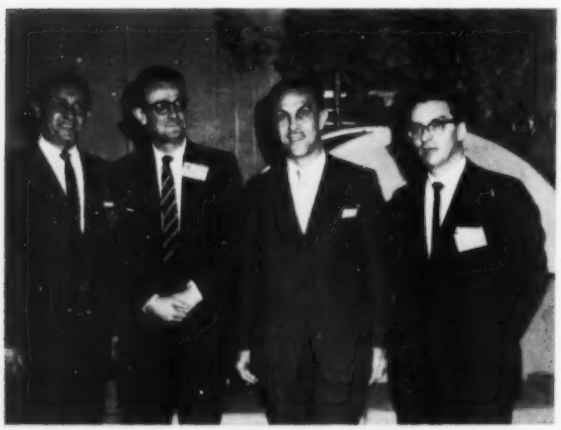
Eugene P. Grisanti has been appointed general attorney for International Flavors & Fragrances, Inc. Mr. Grisanti has been associated with the law firm of Fulton, Walter & Duncombe of New York.

Pictures from the SCC and TGA scientific Meetings

New York City, November 29 and 30, 1960

Martin Brookins, Revlon, Dr. Maury Siegel, Caryl Richards, Dr. Albert Shansky, Rilling Dermetics, Arthur Tarasov, Rilling Dermetics, and Ben Perry, Perry Bros.

Jack McGlynn, and Jane Tucker, Mennen Company, A. G. Nickstadt, Noville Essencial Oil Company, David Jacobs, Mennen Company, and A. H. Moeller, Noville Essential Oil Company.



David J. Warner, Fleuroma, Inc., Dr. Martin Rieger, Warner Lambert Pharmaceutical Co., Frank Buchwalter, Revlon Inc., and A. E. Eisenkraft, Fleuroma, Inc.

Pete Danco of Sun Chemical, Bud Torrey of Chesebrough-Pond's, Mike Spinapolice of Kolmar, Jack Seidler and Larry Driscoll of Whittaker, Clark and Daniels, Inc.

Maurice Raviol, Lautier Fils, Inc., Dr. Henry J. Wing, Chesebrough-Pond's, Inc., and Steve Shyman, Colgate-Palmolive Company.

I. R. Hollenberg, Knapp Products, Inc., and Eustace Fotiu, Avon Products, Inc.

Hays Clark has been elected vice president of international operations of Avon Products, and will transfer to the company's general offices in New York. Clark was formerly manufacturing manager, and will be succeeded by **Robert W. Holmes.**

Robert A. Nielsen has been appointed general sales manager of Estee Lauder Cosmetics. Prior to this appointment, Nielsen had been sales manager of Parfums Givenchy.

Andrew A. Lynn, vice president and a director of Chesebrough-Pond's Inc., has announced his resignation from the firm. He was also president of the corporation's Prince Matchabelli division.

James A. Torrens has been named general sales manager of The Toni Company. Torrens has served as national field sales manager for the past two years.

At the same time, it was announced that the company has promoted two men to newly-created posts in its Sales Division. **Robert F. Bryant** will serve as assistant general sales manager in charge of sales force and field operations and **William F. Frost** as assistant general sales manager for sales development.

John L. Luviano has been elected vice president, machinery division, for Crown Cork & Seal Company, Inc. Mr. Luviano has been with the company for eight years.

Howard Morgens, president of Procter & Gamble Company, received the Annual Award of the Advertising and Allied Industries presented to him as a leading business executive whose contributions to the nation's welfare symbolized the Advertising Industry's concern with the safeguarding of America's democratic legacy. The Award was presented on November 30th at a dinner at the Waldorf-Astoria in New York City.

Edgar W. Nelson, formerly general manager of the Lehn & Fink Division, has been appointed director of marketing for the corporation, in charge of coordinating marketing for the company's consumer products.

Frank H. Orr, formerly assistant to the marketing vice president, has been named assistant to the president of Chesebrough-Pond's Inc.

In addition to handling special assignments for the president, Mr. Straka, Mr. Orr will act as administrative coordinator for the brand managers, the professional products manager, and the market research manager.

Al V. Kuhn, manager of the Hair Color Division of The Realistic Company, heads the Company's brand-new hair color program. Although Realistic has been engaged in hair color research for a long time, official announcement of Kuhn's association with the Color-Kist project comes concurrent with the introduction of this product.

Paul P. Woolard, vice president in charge of marketing for Prince Matchabelli Inc., subsidiary of Chesebrough-Pond's, Inc., has been named executive vice president and a director of the subsidiary. He joined Prince Matchabelli as a salesman in 1950 and after five years was named general sales manager. He became vice president in charge of sales in 1957, and in January, 1959—several months after Chesebrough-Pond's acquisition of the company from Vick Chemical Company—Mr. Woolard was promoted to vice president.

Harold B. Mark has been appointed sales representative for Verona Aromatics. Mr. Mark will represent Verona's full line of aromatics, perfume specialties, and flavors.

Mary Chandler has been promoted to manager of department store sales of Yardley of London, Inc. She fills the position resigned by Marion McDonald upon her marriage.

Miss Chandler joined Yardley one year ago as department store supervisor on the east coast. Prior to her association with the company, she held supervisory positions with Revlon and Helena Rubinstein.

Classified Advertisements

NEW CLASSIFIED RATES

Effective with the January, 1961 issue all classified advertising will be charged at the new rates shown below:

Lightface type—10¢ per word
Boldface type—20¢ per word
Box number—$1 additional
Minimum charge—$2.50
10% discount for advance payment.

Classified display advertising is charged at the rate of $8.00 per column inch for less than ¼ page. Column is 20 picas. ¼ page and over charged at regular advertising rates.

POSITION WANTED

PRODUCTION SUPERVISOR AND DEVELOPMENT CHEMIST. Seeks position with going concern in metropolitan area of New York City. Fifteen year's experience. **Box 6112, AMERICAN PERFUMER, 418 North Austin Blvd., Oak Park, Ill.**

AUSTRALIAN REPRESENTATION? Can you pass up a fast-growing continent? How about heads-up, sensible coverage by a capable man who will live there? It costs nothing to see him before he leaves in March. **Box 6111, AMERICAN PERFUMER, 418 North Austin Blvd., Oak Park, Ill.**

MISCELLANEOUS

COMPLETE SET OF MOLDS for 2, 4 and 8 ounce cologne bottles. Beautiful French design manufactured by T. C. Wheaton Company at cost of $12,000.00. Only used once for one sample run. Will sacrifice $2,500.00 for all three sets. Photographs and specifications sent on request. American Mercantile Company, Inc., 33 West 42nd Street, New York City 36.

PROFESSIONAL SERVICE

"L'ART de la PARFUMERIE par EXCELLENCE"
And its Application to the Industry

DR. JEAN JACQUES MARTINAT
PERFUMER-CHEMIST CONSULTANT

Whatever your problem may be: of a truly original creation or, of a new interpretation of most successful Perfumes per se. Or, of a more recent approach to Fragrances and Flavors for Cosmetics, Toilet Preparations, Pharmaceuticals or Foods, you may confidently discuss it with me on a unique professional level.

Kindly Inquire 333 WEST 52ND STREET, NEW YORK 19, N. Y.
TEL. PLAZA 7-3861

BIO-TOXICOLOGY LABORATORIES
(John Davis Paul, M.D., Memorial Laboratories)

Second Generation of Continuing Service

NORTH BROAD DIV.	CHERRY HILL DIV.
3112 North Broad St.	7703 Maple Ave.
Phila. 32, Pa.	Merchantville 8, N. J.
BAldwin 5-1776	NOrmandy 5-1776

TOXICITY & APPLIED RESEARCH STUDIES
(animal and human)
Prompt replies to inquiries
Toxicity studies initiated within 48 hours of written authorization

GUARANTEED VIRGIN TESTING STOCK
(We maintain our own breeding farms)

RESEARCH AND DEVELOPMENT
Cosmetic Formulation and Improvement

SNELL

Toxicology, skin-irritation studies, analyses and formulations, soap and syndet evaluations. Free booklet: "How to Develop Successful New Cosmetics."

FOSTER D. SNELL, INC.
29 West 15th St., New York 11, N. Y.
WAtkins 4-8800

LEBERCO LABORATORIES
Irritation Studies—Sensitivity Tests
Toxicity and Safety Tests on
Shampoos—Cold Wave Lotions—All Cosmetics
Pharmaceutical and Cosmetic Research
Hormones Assays—Bacteriological Studies
127 HAWTHORNE ST., ROSELLE PARK, N. J.

PAUL BEDOUKIAN, Ph.D.
Consulting Perfume Chemist
Creation or revision of fragrance formulas for the perfume, cosmetic, soap and allied industries.
40 Ashley Road
Hastings-on-Hudson, N. Y. **Tel. Croton 1-4701**

Miniature Perfume Bottles
from ⅛ dram to ½ oz.
Handmade Glass Novelties
Miniature Glass Funnels
SPECIAL ORDER WORK
KENBURY GLASS WORKS
132 W. 14th Street
New York 11, N. Y.

Let **Wrisley** manufacture your

PRIVATE LABEL SOAPS AND TOILETRIES

A CENTURY OF EXPERIENCE IS BEHIND YOU

Fine soap and toiletry items — made to our time-tested formulas or your own prescription. *Distinctively packaged* under your brand name. *Priced for profit* because of our huge production facilities. Phone or write today.

Allen B. Wrisley Company
c/o Private Brand Division 6801 W. 65th Street, Chicago 38, Ill.

TL Beeswax

- PURE WHITE
- EXTRA QUALITY
- ABSOLUTELY PURE
- ABOVE U. S. P. STANDARDS

● Samples will gladly be sent on request—at no obligation

Serving the Trade for 109 Years

THEODOR LEONHARD WAX CO., INC.
HALEDON, PATERSON NEW JERSEY
Western Distributor: A. C. Drury & Co., 219 E. North Water St., Chicago, Ill.

MOULDS for
LIPSTICKS
MASCARA
SUPPOSITORIES
STYPTIC PENCILS

and **DIES** for
ROUGE
COMPACT POWDER

Write for Catalog

A. CAVALLA, INC. 163 West 18th Street, New York, 11, N.Y.

WE BUY FOR CASH
CLOSE-OUTS • SURPLUS

Bottles • Caps • Jars • Containers • Chemicals • Closures
Cosmetics of any Descriptions
Also Business Small or Large . . .

UNIVERSAL OUTLET CO.
1 E. 15th St. • New York 3, N.Y.
Telephone Oregon 5-9444—
Oregon 5-8568

Index OF ADVERTISERS

SOOTHING WORDS

...that give sales a lift

"Contains Glycerine" is an appealing phrase to millions of American women. It brings to mind the soothing skin softness produced by Glycerine and Rose Water, Glycerine Soap and other long familiar products. It's an extra that promotes sales on any label . . . indicating high-quality ingredients of assured safety.

Glycerine is thoroughly acceptable and compatible in toilet goods. In addition to its well-known humectant action, it controls body and consistency, lubricates, prevents settling, resists hardening and prolongs product life...an unmatched combination of desirable properties.

A group of toilet goods experts discussed "Glycerine in Toilet Goods" at our 1960 Symposium. We'd be pleased to send reprints of their talks. Address your request to the Glycerine Producers' Association, 295 Madison Ave., New York 17, N. Y.

ADVANTAGES THAT COME WITH . . .
Glycerine

RISDON VALVE QUALITY IS VITAL INSURANCE

The payoff point for all the time and money invested in your aerosol product is at the fingertips of the user. That is where repeat sales are made or lost.

When your customer pushes the actuator, the performance-insuring quality of a Risdon valve becomes vital. And nothing less than Risdon quality gives full assurance of customer-pleasing results over the entire life of the package. An inferior valve can turn out to be your most expensive "bargain".

Risdon quality... performance-proven on many millions of packages... is the result of extensive scientific research and development. It is zealously guarded at every stage of valve manufacture by Risdon's uncompromising quality control.

Most *leading* aerosol packagers keep their success secure by using only Risdon valves to dispense their products.

Contact Risdon for specific information on the valve for your product.

Write For Free Booklets
On RISDON Valves

FOR Pressurized Products Packaged in Glass, Metal or Plastic Containers.

DISPENSING Conventional Aerosols, 3-Phase Products, Alcohol Base Products, Water-Base Products, Foam Products, Powder Sprays, Metered Sprays, Ultra-Low Pressure Applications, Products Containing Propellent Emulsions or Dispersions, etc.

RISDON

THE RISDON MANUFACTURING CO.